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Bulk Polymerization and Structure-Property Relationship of Medical Grade Polyurethane

Mariam Nasser Al-Saedi

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United Arab Emirates University
Deanship of Graduate Studies
M.Sc. Program in Material Science and Engineering

Bulk Polymerization and Structure- Property Relationship of Medical Grade Polyurethane.



By:

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A thesis submitted to the deanship of graduate studies in partial
fulfillment of the requirements for the Degree of M.Sc. in Materials
Science and Engineering

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May ٢٠٠٤

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All thanks are due to Almighty Allah for his blessings and for providing me the capability to successfully complete this work.

To my first valentine,

I would like to take this opportunity to thank my senior supervisor, Dr. Mahmood Mohsin, who planned and supervised this research project. His sincere guidance,

encouragement, fruitful discussions, critical reviewing and assistance during the various phases of this work greatly aided its completion.

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My thanks also goes to the staff of the central laboratories unit (CLU) for their cooperation in testing the polymer samples. Especially Mr. Essam Attia in the SEM lab, Mr. Jamal and Mr. Hussain in the FTIR and NMR labs respectively. Also my thanks extend to Mr. Ali Dewidar in the chemical and petro lab, who carried out the DSC scans.

Your loving sister

Finally my greatest deep of gratitude is due to *Mariam Nasser Al-Saedi* my friends inside and outside the University for their unfailing support throughout my study.

No words can ever express my great gratitude and special thanks to my loving family especially my parents, brothers and sisters for their continuing love and support throughout my academic career. Thanks to their patience and for taken good care of me.

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Abstract

Polyurethanes as biomaterials have been used in the augmentation and repair of the human body with great success. The choice of material for a particular application often hinges on the body's response to the polymer, the mechanical and thermal properties of the polymer and the stoichiometric ratio of active ingredients used in the synthesis.

A large number of polyurethanes used in medical applications are polyester-based and cannot be used in long-term implant applications because they are very susceptible to hydrolysis. Other medical-grade polyurethanes, which are suitable for implants are polyether-based which might to some extent, suffer from environmental stress cracking (ESC), thus adversely affecting the mechanical properties of the polymer in the long run. Such degradation is due to enzymatic attack on the polymer, enzymes that are secreted by macrophages, which are part of the body's immune response to foreign substances. Once initiated, micro-cracks can propagate and lead to potentially catastrophic device failure. What seems to be emerging as the answer to some of these problems are polycarbonate-based polyurethanes that have demonstrated resistance to environmental stress cracking.

Polyurethanes have found applications in the domains of medical devices, drug delivery, heart valves, catheters and the most dramatic and successful development is in the artificial hip prosthesis. Most of these applications depend on the excellent properties that can be achieved with controlled polymerization processes and their methodology. Polycarbonate-based polyurethane is considered to be a block co-polymer consisting of alternating hard and soft segments. Its bulk properties are generally attributed to the nature and extent of phase separation.

The unique aspect of a polyurethane, is that it can be tailor-made with specific properties solely by altering the ratio of the main components of the polymer's molecular structure (crystalline and amorphous segments) without the need for catalysts, plasticizers, additives, or reinforcing agents

In this study, linear polyurethanes with a range of formulations based on soft-to-hard segment ratios were synthesized in bulk using Diphenylmethane-4,4'-diisocyanate (MDI), Butandiol (BD) as chain extender, and Polycaprolactone diol (PCL) with varying molecular weights. The variations in polyurethane properties that can be obtained during synthesis were characterized using Thermogravimetric Analysis (TGA), Fourier

Transform Infrared spectroscopy (FTIR), Nuclear Magnetic Resonance spectroscopy (NMR) and Differential Scanning Calorimetry (DSC).

Biocompatibility tests were investigated for some polyurethane samples in order to check if these polyurethanes were suitable for the desired medical application such as hip prosthesis. The results were analyzed using both Scanning Electron Microscopy (SEM) for the polyurethane samples and Optical Microscopy (OM) for the biological tissues.

The main finding was that some polyurethane samples with uniform distribution between hard and soft segments had the lowest adverse biological effect. Some samples caused severe irritation in the tissue and a lot of surface erosion in the polymer sample. This can be traced to the polyurethane composition and the curing process used in the preparation of these samples.

It is concluded from experimental results that the properties of polyurethane samples depend on their structure, which can vary according to their composition. It was found that two sets of tested polyurethane samples were biocompatible and one set was not.

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Abbreviations

DSC	Differential Scanning Calorimetry
FTIR	Fourier Transform Infrared Spectroscopy
MDI	4,4'-diphenylmethane diisocyanate
MDICL	MDI + Polycaprolactone diol
MDIDPEGA	MDI + Dipoly(ethyl glycol)adipate
MDIPEG	MDI + Polyether glycol
MDIPPG	MDI + Polypropylene glycol
M_n	Number Average Molecular Weight
NMR	Nuclear Magnetic Resonance
OM	Optical Microscopy
PU	Polyurethane
SEM	Scanning Electron Microscopy
TDI	Toluene diisocyanate
T_g	Glass transition temperature
TGA	Thermogravimetric Analysis
T_m	Melting temperature



Chapter One

Introduction



Introduction

1.1. Definitions:

During the past four decades, there have been many successful attempts to extend and improve the quality of human life. The development of artificial joints is but one example; such devices manufactured from synthetic polymers have become an important part of orthopedic health care programmes

This development has an integral role in bringing together professionals from different fields such as medical device manufacturers, medical polymer suppliers, designers, physicians and surgeons [1].

Artificial joints are biomaterials that have to be compatible with the human body. Biomaterials are artificial materials that are designed for biomedical applications, or they are materials of natural or man-made origin that are used to direct, supplement or replace the functions of living tissues of the human body [2]. They can safely be implanted into the human body and left there without causing an adverse reaction. Biocompatible material can be defined as material that has to be compatible with the living tissue into which it is implanted or with which it is brought in contact. Where as incompatible materials lead to cytotoxic reactions or immunological rejection. [3].

For successful usage of polymer as biomaterials in medical devices, there are six general considerations which have to be taken into account:

I. Biocompatibility: which covers a two-way interaction with the material itself:

- (a) Implant material should not be affected by the physiological environment.
- (b) Local tissue and organs should not be harmed by the presence of the implant material.

Adverse effects on the biomaterial are corrosion of metal and erosion of ceramic implants, or degradation of polymers by the body's saline solution. Adverse effects on tissues are mainly unfavorable cellular reactions, and synergistic action of the implant with bacteria to cause infection.

II. Sufficient mechanical properties:

The implant materials may be subjected to loads and stresses which can be high, or cyclic in nature, and at different strain rates. These materials therefore should have mechanical properties such as yield, ultimate strength, ductility, modulus of elasticity and viscoelastic behavior to perform well in such environments [3].

III. Low friction and wear:

As a result of prolonged usage of artificial joints, their friction and wear properties change ultimately affecting high wear resistance.

IV. Dimensions appropriate to its location:

Implant materials must cause no undue damage like in-knee prosthesis, it must have an appropriate volume that would cause the least degree of irritation to surrounding tissues.

V. Long-term functionality:

Which means that the implant material must fulfill its intended function over the whole lifetime of the patient if it is a permanent implant or until its purpose is achieved [3,4].

VI. Sterilization:

There are many methods for sterilizing biomaterials such as : autoclaving (by using steam at 120° to 140° C), gamma radiation, or sterilization by ethylene oxide, such methods must not affect the material properties.

Requirements of Biomaterials:

Implant materials must not cause the following:

- Degradation of cellular elements (red and white blood cells)
- Alteration of plasma proteins.
- Enzyme denaturing.
- Damage to adjacent tissue.
- Activation of the complement system.
- Destroy the biological environment by changing the physical, chemical, mechanical or surface properties [4,5].

A new family of biocompatible polymers called polyurethanes have emerged with their unique physical and mechanical properties which are considered the best choice for a number of biomedical applications. Polyurethanes (PU's) are polymers that contain urethane linkages $[-\text{ROOCNH}-\text{R}'-]_n$ in their backbone, where R represents an alkyl group that is different from R' (an alkyl group is an organic group obtained by removing a hydrogen atom from an alkane).

Polyurethanes can be found in elastomers, fibers, rigid foams, flexible foams, industrial parts, industrial materials, sports goods, medical equipment, coatings and adhesives. Rigid polyurethanes are used as insulation material for buildings (such as those for filling wall cavities in houses), water heaters, commercial, domestic refrigerators and for general energy management, while flexible polyurethanes are used as underlay cushioning for carpets, soft furnishing, automobiles and for packaging [6]. Polyurethane adhesives are used in construction, transportation and other applications that require high strength, moisture resistance and long life-time [6,7]. Most of the above applications use

polyurethanes which are crosslinked and thus possess thermosetting plastic properties. Some Polyurethanes though have a linear molecular arrangement which does not cross-link leading to formation of thermoplastic materials which can be reinforced or nonreinforced.

1.2. Classifications of Polyurethanes:

1.2.1. Thermosetting polyurethanes:

Thermosetting polyurethanes are polymers that can be heated to a point where they would soften and could be made to flow under stress (load). Upon further heating to relatively high temperature, the polymer starts to degrade [8]. These polymers are used in various forms, such as soft foams which are used to make seat cushions, mattresses, and packaging materials or as hard foams that are used as insulation in refrigerators, freezers, water boilers and homes.

1.2.2. Thermoplastic polyurethanes:

Thermoplastic polyurethanes are polymers that would soften upon heating and could then be made to flow when a stress is applied. When cooled, they would reversibly regain their solid or rubbery nature. They have linear, highly crystalline molecular structure which makes them abrasion-resistant. This type of polyurethanes are molded in shoe soles, car fenders, door panels and other products. Thermoplastic polyurethanes are the most important implantable-grade polyurethanes used in medial applications [8,10].

1.3. Polyurethanes composition:

Polyurethanes are made up of hard and soft segments. The hard segment comes from the extension of a diisocyanate with a low-molecular-weight diol, and the soft segment from the crosslinked network polyester or polyether [11,12].

Polyurethanes are elastomeric materials produced by the bulk one-pot polymerization approach of diisocyanate and polyols [13]. This approach has the advantage of scaling-up

yielding polymers with varying degrees of branching without formation of by-products [14].

The three main constituents of Polyurethanes [15] are:

- (I) A diisocyanate (such as MDI) 4,4'- diphenyl methane diisocyanate,
- (II) A long-chain (high molecular weight) polyol either as a polyester or as polyether.
- (III) A chain extender (low molecular weight) which is a short-chain glycol or a diamine.

The reaction between diisocyanates (or polyisocyanates) that have more than one reactive isocyanate group per molecule and difunctional alcohols (or Polyfunctional alcohols) with two or more reactive hydroxyl groups or amines will give polyurethanes and polyureas respectively [16].



Diols and diisocyanates produce linear polyurethanes. Triols, triisocyanates and monomers of higher functionality produce branched and cross-linked polyurethanes. This reaction is classified as nucleophilic which involves attack on the central carbon atom of an isocyanate (-N=C=O) by a compound having an active atom (oxygen or nitrogen) such as a diol or an amine [14]. The reactivity of the isocyanate is increased by the presence of electron withdrawing groups attached to the double bond system. This makes aromatic isocyanates more reactive than aliphatic ones [17]. Table 1.1 shows typical polyols used in the preparation of Polyurethanes.

Table 1.1: Various types of polyols.

Chemical structure	Chemical name
$\text{HO}-(\text{-CH}_2\text{CH}_2\text{O-})_n\text{-H}$	Polyethylene oxide (PEO)
$\text{HO}-(\text{-CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{-O-})_n\text{-H}$	Polytetramethylene oxide (PTMO)
$\text{HO}-(\text{-C}(\text{CH}_3)_2\text{-CH}_2\text{-})_n\text{-OH}$	Polyisobutylene (PIB)
$\text{HO}-(\text{-CH}_2\text{-CH=CH-CH}_2\text{-})_n\text{-OH}$	1,4-polybutadiene (POD)
$\text{HO}-(\text{-CH}_2)_4\text{-(Si(CH}_3)_2\text{-O-})_x\text{-Si(CH}_3)_2\text{-(CH}_2)_4\text{-OH}$	Polydimethylsiloxane (PDMS)
$\text{H[-O(CH}_2)_5\text{CO-}]_n\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{O[-CO(CH}_2)_5\text{O-}]_n$	Polycaprolactone diol (PCLD)

There are different types of isocyanates that are used in the preparation of polyurethanes. Table 1.2 provides a few examples.

4,4'-diphenylmethane diisocyanate (MDI) has superior reactivity and polymers based on MDI may possess better physical properties than other isocyanates. Also, MDI is crystallizable which means that MDI-based hard segments can readily crystallize under the right conditions.

Table 1.2: Polyfunctional Isocyanates Used to Prepare Polyurethanes

Structure	Average functionality	State at room temperature	Normal state of use	Important uses
Polymeric types from MDI	2.5 – 3.2	Liquid	Liquid	Foams
Biuret-modified 1,6-hexamethylene diisocyanate	3	Viscous liquid	Solution	Coatings
Isocyanurate-modified TDI	2 – 3	Liquid	Liquid - Solution	Coatings
Triphenylmethane triisocyanate	3	Solid	Solution	Coatings
Carbodiimide-modified MDI	> 2	Liquid	Liquid	Foams
TDI adducts	Approx. 3	Solid	Solution	Coatings
Lysine isocyanate adducts	Approx. 3	Solid	Solution	Coatings

Typical chain extenders are shown in table 1.3:

Table 1.3: Typical chain extenders.

Chemical structure	Chemical name
$\text{HO-CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{-OH}$	1,4-butanediol
$\text{H}_2\text{N-CH}_2\text{CH}_2\text{-NH}_2$	Ethylene diamine
$\text{HO-CH}_2\text{CH}_2\text{-OH}$	Ethylene glycol
$\text{HO-(CH}_2)_6\text{-OH}$	Hexanediol [18]

Polyurethane hard-segment chain extenders can be classified into two general classes, which are aromatic diols and diamines and the corresponding aliphatic diols and diamines. In general aliphatic chain extenders yield softer materials than do aromatic chain extenders. This is due to the tendency of hard segments containing aromatic chain extenders to possess a greater volume fraction of hard segment material.

Polyols available for polyurethane synthesis include polyethers, polyesters, polyalkyls, and polydimethylsiloxanes. Traditionally, polyurethanes have been produced with polyether and polyester soft segments. Polyester based urethanes possess relatively good material properties. Polyether based urethanes exhibit a relatively high resistance to hydrolytic cleavage [16].

Polyols give high flexibility to the backbone of the network chains and therefore are called soft domains or soft segments. While isocyanate and chain extender components give rigidity to the chains and are called hard domains or rigid segments.

For stepwise cross-linking (cure) reactions, the three most common additives are 1,4-butanediol, diamine, and water (which acts as chain-extender) and/or cross-linking

agents, depending on the functionality of the prepolymer and the overall stoichiometry of the reaction [16].

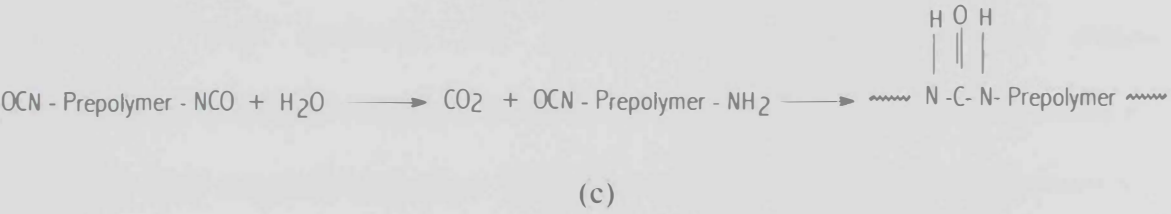
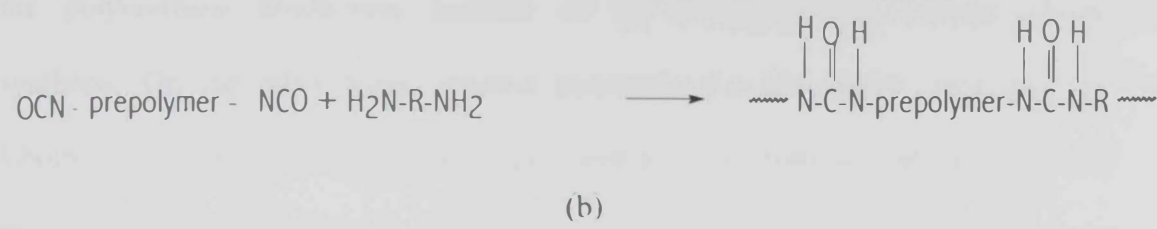
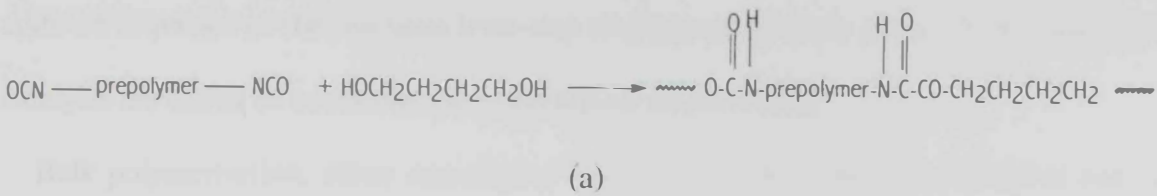


Figure 1.1: Cross-linking using (a) 1,4-butandiol (b) Diamine (c) Water

There are two types of crosslinking, physical and chemical crosslinking. Physical crosslinking occurs by hydrogen bonding and hard domain formation, which develops because the soft segments consisting of the polyols are incompatible with the hard segments containing the diisocyanate part. The hard segments act as both physical crosslinks and fillers [19].

Chemical crosslinking can be introduced into the system in many ways, but common methods include using a triol or higher functional polyol and having an isocyanate-to-hydroxyl (NCO/OH) ratio greater than 1, in which the excess isocyanate groups react with urethane groups to form allophanate linkages [19].

1.4. Polyurethanes preparation methods:

The various methods for producing segmented polyurethane elastomers can be differentiated according to the medium of preparation (bulk, solution, water) and the addition sequence of the reactants (one-step process, prepolymer process). In some cases, catalysts are added to accelerate the polyaddition reaction [20].

Bulk polymerization, either one-step or two-step, has been the main industrial process for polyurethane production, because of its environmentally friendly solvent-free synthesis. On the other hand, solution polymerization has largely been used for the laboratory or experimental synthesis of polyurethanes. As expected, different synthetic processes have an effect on both rate and yield. For example, in some types of polyurethane bulk synthesis, the incompatibility between reactants induces polymerization to form a heterogeneous system or the system becomes heterogeneous at a relatively early stage of the reaction. Therefore, the composition of the final product is controlled by the diffusion rate of the reactants from one phase to the other. Solution polymerization can also be a one-step or two-step process. In one step synthesis, the reaction is carried out by simultaneously mixing a polyol, a diisocyanate, and a chain extender together in the reaction solvent and heating the solution above 80°C. In some cases, catalysts are applied to accelerate the reaction [20].

However, the more common route of making polyurethane is via the two-step synthesis, or prepolymer route. In this method, the first step is to react the polyol with excess diisocyanate to form a diisocyanate terminated intermediate oligomer, i.e. a prepolymer, with a molecular weight of 1000 to 5000 g/mol, depending upon the polyol's molecular weight and the ratio between these two reactants. The prepolymer that is formed is normally a viscous liquid, or a low-melting-point solid, which is easily stored. The second step is to convert this prepolymer to the final high molecular weight

polyurethane by further reaction with a diol or diamine chain extender. This step is usually referred to as chain-extension. [5]

A polyurethane structure made by the two-step method tends to be more regular than the corresponding polyurethane made by the one-step method. This is because the two-step method caps the polyol with diisocyanate and then connects these oligomers with chain extenders. The polymer chain has a more regular hard-soft-hard sequence than seen in the random distribution of hard segments in the one-step process. Therefore, the hard segment size distribution is narrower than in the one-step method. This structural regularity may impart better mechanical properties to the polyurethane since the hard segments more easily aggregate or crystallize to form physical crosslink points [21].

Polyurethanes can be prepared by two basic processes. Mixing all the reactants at once (one pot process) provides the fastest, simplest and most economical manufacturing technique to mix a liquid diol, a polyol, and diisocyanate and to cast the mixture in a mold while still liquid. Casting of the mixture yields an elastomeric product with random distribution of soft and hard segments [16]. To obtain a thermoplastic elastomer, the reactants should be chosen such that they produce a linear structure. This is called a *one-shot process*.

The second method involves the reaction of a linear hydroxy-terminated polymer with an excess of diisocyanate to form an isocyanate-terminated polymer called a *prepolymer* which is either a viscous liquid or a low-melting solid. This prepolymer then reacts with a small molecular weight polyol or amine called a chain extender in order to extend the chains and form a network as shown in figure 1.2 and 1.3 [16].

The two steps or three step processes give much greater control over tacticity, reactivity, structure, properties, processability and finished product quality. In a typical two steps process, the first step is production of a prepolymer:



Figure 1.2: Formation of prepolymer.

The second step is reaction of the prepolymer with a chain extender such as a diol or a diamine.



Figure 1.3: Formation of polyurethanes.

In many cases, controlled cross-linking is introduced as the second or third step; to produce a high molecular weight polymer [16].

Devices of polyurethane products are readily manufactured by almost all of the traditional manufacturing methods including extrusion, injection molding, thermoforming, and blow molding (for thermoplastics) and lay-up, spray-up, compression molding, and casting (for thermosets).

1.5. Applications of polyurethanes:

Polyurethanes are used as biomaterials for the fabrication of medical implant devices such as blood filters, catheters, heart valves, cancellous bone substitutes, cardiac-assist devices, drug delivery accessories and hip prosthesis. They are used for short-term in-body resident devices, medium-term life-support blood external treatment components (systems for dialysis), and long-term implanted artificial device components (artificial heart ventricles, pacemakers and neurological pacing leads, heart valve leaflets) [22-25].

Polyurethanes are also used in resins, protective coatings, insulation, adhesives, foams, fibers used in stretch clothing, decorative coatings which exhibit high gloss, hardness and toughness which is the ability of the material to absorb energy without

breaking and it can be measured from the area under the stress-strain curve of that material [26].

1.6. Polyurethanes Properties:

This wide field of applications resulted from the excellent physical, and mechanical properties of Polyurethanes such as high strength, flexibility, fatigue resistance, hardness in the range from 20 shore A (softer than a gum eraser) to over 80 shore D (harder than a golf ball), high elongation modulus at break, better impact resistance than almost all plastics, excellent resistance to tear (strong indicator of toughness) and to most types of fluids [27-29]. They possess desirable electrical properties such as good adherence to electrodes, are very good insulators used in many potting and encapsulating applications and have the ability to mix homogeneously with many inorganic salts [30]. These polyurethanes can vary from light and flexible, as soft as skin for furniture, car seats and packing, to strong and rigid, as hard as bone for elastic fibers and molding materials. They can outperform steels and rubbers for abrasion resistance and can be molded to any shape [6,13].

They are unique materials that have the elasticity of rubber combined with the toughness and durability (the capacity of the material to survive its intended use for a suitably long period of time.) of metals.

Polyurethanes can replace rubber, plastics or metals due to their durability, which means that they can be made of less material and weight, reducing maintenance and cost. In addition, they have high load bearing properties in tension, compression, and shear. They also have a coefficient of friction varying from very low, for items like bushings, bearings, to very high, for items like tires or rollers.

Polyurethanes decompose at around 220°C and thus maintain their properties at body temperatures [31]. They also have good resistance to thermal shock, can withstand sudden

temperature drops without cracking and remain flexible at very low temperatures which is required for some applications. They have good optical properties are biologically stable, [32] have high resistance to gamma rays and are stable at high-humidity or in tropical environments [16,33].

Strong polarity and hydrogen-bonding make polyurethanes highly resistant to hydrocarbon fuel and oil and make linear polyurethanes dissolve, and cross-linked polyurethanes swell in polar organic solvents. This is useful in solution processing of fibers, coatings, and adhesives.

1.7. Advantages of Polyurethanes:

In addition to the already mentioned properties of polyurethanes, they also have excellent resistance to oils, solvents, fats, greases and gasoline with high tear strength which is superior to rubbers. They have outstanding resistance to atmospheric oxidation (oxygen and ozone due to their saturated structure), sunlight and have excellent electrical insulating properties and thus are used in many molded wire and cable harness assemblies. With higher load bearing capacities (in both compression and shear) than any conventional rubber, polyurethanes are used in high load bearing wheels, metal forming pads, stripper springs, press in solid tires and heavy duty couplings polyurethanes as well have excellent abrasion resistance properties [29,34].

1.8. The Objectives and Impact of the study:

This thesis addresses the synthetic method of segmented thermoplastic polyurethane with which was intended to improve its wear resistance and also its large-scale synthesis using bulk polymerization. A number of linear polyurethanes were prepared from MDI, Polyol and chain extender. These polymers displayed a complex two-phase morphology and composition-dependant mechanical and thermal properties. The PU segment microphase separated from other polyurethane segments and varying

microphase separation morphologies were observed. Similar thermal stability was observed for both the commercial polyurethane and the synthesized polyurethane in this work.

Thermoplastic polyurethanes are a versatile group of multi-phase segmented polymers that have excellent mechanical and elastic properties, good hardness, high abrasion and chemical resistance. As well, they have unique thermal properties of a kind not seen in other polymers. The increasing demands for polyurethanes for medical devices have stimulated the development of new materials.

This research focused on producing thermoplastic polyurethane biopolymer with potential uses in hip replacement as an acetabular cup lining without significantly sacrificing its excellent mechanical properties. This was approached via bulk polymerization without the need for catalyst or co-catalyst since leaching of unreacted materials may cause inflammation to the host organ in the human body. Structural, thermal, morphological, surface, and hardness characterization of the products are presented.

The performance and biocompatibility of every new material must be very well confirmed before it can be accepted into use as an implant material. The main purpose of the present study is to synthesize medical grade polyurethanes and examine their biocompatibility and thermal properties.

To fulfill this objective, the following items are considered:

- To establish well-defined routes for controlled polymer synthesis in bulk process.
- To study the thermal properties of polyurethane samples.
- To investigate the chemical structure of polyurethanes.

- To establish a specific formulation and process in order to satisfy specific thermal properties.
- To investigate the effect of the implant on living tissue (rat skin).
- To explore the morphological structure of the polyurethane samples before and after implantation in rats' skins.

1.9. Tasks:

Several tasks are required in carrying out this study. These include:

- Carrying out a literature review to gather information on the chemistry and structure-properties relationship of the polyurethanes.
- Studying the characterization and different properties of the polyurethanes.
- Devising an experiment to study the biocompatibility of the polyurethanes.
- Analyzing the experimental data and discussing the results in order to match the properties to the structure and composition of the polyurethanes.

The tasks of this study had been done in four main laboratories, which are

- (a) Chemistry Laboratories, UAE University, where the synthesis of the polyurethane samples with different compositions (ratio) had been carried out.
- (b) Central Laboratories Unit (CLU) where the chemical (structure) analysis of the polyurethane samples using Nuclear Magnetic Resonance (NMR) and Fourier Transform Infra Red (FTIR) with Thermogravimetric analysis (TGA) were done. Also, the morphological characterizations of the treated and untreated polyurethane samples were examined by using Scanning Electron Microscopy (SEM).
- (c) Physiological Laboratory, Faculty of Medicine, where the processing, staining and mounting procedures of the tissues were carried out.
- (d) Biological

Laboratory, UAE University, where the implantation of the polyurethane samples and the tissue reactivity were analyzed using Optical Microscopy (OM).

1.10. Thesis Organization:

This thesis is divided into five chapters. Chapter one includes the general introduction of biocompatible materials, polyurethanes, their properties and applications. In addition to the purpose and significance of the study with the required tasks to fulfill these objectives. As well as, the different laboratories where the experiments had been done were mentioned. Also, the outline of the thesis was displayed.

A literature survey of the polyurethanes is presented in chapter two. It includes polyurethanes chemistry, the raw materials in polyurethanes syntheses such as isocyanates, polyols, and chain extenders as well as other additives. Furthermore, it covers the general principles in the structure-property relationship of polyurethanes. The thermal, electrical and optical properties of polyurethanes were described.

Chapter three includes the experimental methodology of this thesis. It contains the materials used in the synthesis of polyurethanes with their sources. As well as, the two-shot bulk polymerization reaction between the raw materials. The main part of this chapter is the material characterizations, which include:

- Thermal analysis techniques to test the thermal transitions of the polyurethanes such as Thermogravimetric analysis (TGA) and Differential Scanning Calorimetry (DSC).
- Chemical analysis to identify the chemical structure of polyurethanes such as Nuclear Magnetic Resonance (NMR) and Fourier Transform Infra Red analysis (FTIR).

The histology experiment was described at the end of this chapter followed by the techniques used to investigate the response of the polymer samples which are Scanning

Electron Microscopy (SEM) and the Optical Microscopy (OM) to check the biocompatibility of the polyurethanes samples by implantation in the rats skin.

Chapter four presents the results and discussion of the analysis of the polyurethane samples. Thermal properties which were investigated by using TGA and DSC showed that the polyurethanes were stable in a wide temperature range which make them suitable for the required medical application. NMR and FTIR confirm the structure of the polyurethane samples. In addition, the implantation effect and the tissue reactivity in biological skin were analyzed. The analysis of implanted polyurethanes samples and skin tissue were discussed. In this context, the results indicate that some polyurethanes samples were better than others against the implantation and biological activities.

Chapter five covers the general conclusion with further recommendations. It summarizes the results of the experiments and presents suggestions for future research on the appropriate use of these polymers as biomaterials.



Chapter Two

Literature Review



The major research areas involved in this thesis are presented in this chapter. These areas include segmented thermoplastic polyurethanes and polyurethanes in medical applications.

2.1. Segmented Thermoplastic Polyurethanes:

2.1.1 History and Development of Polyurethanes

The invention of polyurethanes was made by Otto Bayer and coworkers at I. G. Farbenindustrie, Germany in 1937 [35]. This discovery was Germany's competitive response to Carothers' work on polyamides, or nylons, at E. I. du Pont. The successful development of high molecular weight polyamides at E. I. du Pont stimulated Bayer to investigate similar materials that were not covered by Du Pont's patents. The initial work was to react an aliphatic isocyanate with a diamine to form polyureas that were infusible, but very hydrophilic. Further research on this subject demonstrated that when an aliphatic isocyanate reacted with a glycol, a new material with interesting properties for production of plastics and fibers could be made. Du Pont and ICI soon recognized the desirable elastic properties of polyurethanes. The industrial scale production of polyurethane started in 1940 [36] but subsequent market growth of these materials was seriously impacted by World War II.

The polyurethane elastomers that were first developed consisted of three components:

- (a) Polyester and polyether based macrodiols (eg. M_n of 1-2000g/mole)
- (b) Chain extender such as low molecular weight diol or diamine
- (c) A bulky diisocyanate, i.e. naphthalene-1,5-diisocyanate (NDI)

The polyurethane elastomers made from these components were not thermoplastic elastomers in the true sense, since their melting points were higher than the decomposition temperature of the urethane linkages. It was not until 1952, when polyisocyanate, especially toluene diisocyanate (TDI), became commercially available,

that noticeable improvements in polyurethane elastomers and foams began to be seen. In 1958, Schollenberger of BFGoodrich introduced a new "virtually crosslinked" thermoplastic polyurethane elastomer [37]. At approximately the same time, du Pont announced a Spandex fiber called Lycra, which is a polyurethane based on polytetramethyleneoxide (PTMO), 4,4'-diphenylmethane diisocyanate (MDI) and ethylene diamine. By the early 1960s, BF Goodrich produced Estane, Mobay marketed Texin, and Upjohn marketed Pellethane in the United States. Bayer and Elastgran marketed Desmopan and Elastollan, respectively, in Europe.

In addition to elastomers, polyurethanes can also be produced as foams (rigid and flexible), adhesives, binders, coatings, and paints. Because of their unique properties, polyurethanes have found a wide variety of applications as previously mentioned in chapter 1.

In 1990, the world production of plastics exceeded 100 million tons. Following the high volume production of thermoplastics such as polyethylene (PE), polyvinylchloride (PVC), polypropylene (PP), and polystyrene (PS), polyurethanes rank 5th with over 5% of the world's total plastics production.[20]

2.1.2 Polyurethane elastomers

Polyurethane elastomers are an important member of the thermoplastic elastomer family[4]. Although the consumption of polyurethane elastomers is lower than that of polyurethane foam, they are used for variety of unique applications that are inappropriate for other polymers. Their advantageous properties include high hardness for a given modulus, high abrasion and chemical resistance, excellent mechanical and elastic properties, and blood and tissue compatibility. Generally, polyurethane block copolymers are comprised of a low glass transition or low melting "soft" segment and a rigid "hard" segment, which often has a glassy T_g , or crystalline melting point well above room

temperature. The soft segment is typically a polyester-, or polyether- diol, with a molecular weight between 500 to 5000 g/mol, though in practice, molecular weights of 1000 and 2000 g/mol are primarily used. The hard segment normally includes the connection of a diisocyanate (aromatic or aliphatic) and a low-molecular-weight diol or diamine, which is the chain extender. The combination of this soft polyol segment and hard segment forms an (AB)_n type block copolymer. By varying the structure, molecular weight of the segments, and the ratio of the soft to hard segments, a broad range of physical properties can be obtained. The materials can be hard and brittle, soft and tacky, or anywhere in between [20].

Polyurethane elastomers usually exhibit a two-phase microstructure, which arises from the chemical incompatibility between the soft and the hard segments. The hard, rigid segment segregates into a glassy or semicrystalline domain, and the polyol soft segments form amorphous or rubbery matrices in which the hard segments are dispersed at varying content levels. The hard domain in this two-phase microstructure can act as a physical crosslinking point and reinforcing filler, while soft segments behave as a soft matrix. This microphase separation results in superior physical and mechanical properties, such as high modulus and high reversible deformation. The degree of phase separation or domain formation not only depends on the weight ratio of the hard to the soft segment, but also on the type of chain extender, the type and molecular weight of the soft segment, the hydrogen bond formation between the urethane linkages, the manufacturing process, and reaction conditions.[20,5] This phase segregation behavior of polyurethanes has been well established by a variety of characterization techniques, including electron microscopy, small angle X-ray scattering, infrared dichroism, dynamic mechanical analysis, and differential scanning calorimetry [38].

2.2. Polyurethanes synthesis and characterization methods; some literature survey:

Ludovic Valette and et.al. [11] synthesized polyurethanes from 4,4'-diphenylmethane diisocyanate (MDI) and unsaturated polyester polyol using free-radical polymerization for studying the influence of hard domains on mechanical properties of the polymer products. Heat distortion analysis, dynamic mechanical analysis, flexural three-point bend tests and unnotched Izod impact analysis were used for the characterization. They found that the phase-separated hard domains acted as virtual crosslinks and reduced the number-average molecular weight between crosslinks. Hexanediol chain extenders increased the flexibility of the polymer chains, resulting in higher deformation and impact resistance of the polymer. While ethylene glycol chain extenders showed poor ultimate mechanical properties due to the formation of phase-separated hard domains.

Silvia Fare and et.al. [24] used commercial polymers to study the stability of polyetherurethanes (PEUs) and polycarbonateurethanes (PCUs) under strong oxidative conditions (0.5N HNO₃, pH 0.3; and NaClO, 4% Cl₂, pH =13) using Differential Scanning Calorimetry (DSC), Gel Permeation Chromatography (GPC) and Fourier Transform Infra Red Spectroscopy (FTIR). They concluded that the use of sodium hypochlorite seems to be more effective in creating an environmental stress cracking (ESC)-like degradation for polyurethanes that resists other aggressive chemical environments.

B. Bogdanov and et.al. [39] used polycaprolactone diols (PCL) with different molecular weights (2000 and 4000) with 1,1'-methylene-bis(4-isocyanateocyclohexane) to synthesize poly (ester-urethanes) (PEUs) for studying the physical properties of the resulting polymers. They found that there was a heterogeneous structure consisting of a continuous PCL matrix with a hard segment dispersed rigid phase. The crystalline phase,

which developed in PEUs, is due to the PCL soft segment crystallization and from the DSC analysis, the glass transition temperature T_g of the segmented PEUs was greater than that for PCL prepolymer due to the decrease in flexibility imparted by the hard segments. The physical properties of the PEUs depend on the different procedures for sample preparation (precipitation, casting from solution and melt crystallization).

J. K. Haken and et.al. [15] used commercial polyether- based polyurethane which was cleaved into the corresponding diamine, polyether, diol, or hydrocarbon by molten alkali fusion at high temperature. These fragments were analyzed using Gas and Gel Permeation Chromatography (GC and GPC). A mixed anhydride reagent was used to cleave the polyether into corresponding polyol acetates for GC analysis.

Kezban Ulubayram and Nesrin Hasirci [1] synthesized polyurethanes from 2,4-toluene diisocyanate (TDI) and polypropylene glycol (PPG). They concluded that the samples with higher TDI to PPG ratios had higher tensile strength, lower ultimate elongation and lower oxygen permeability due to the presence of hard segments (TDI), which reduce the flexibility of the chains. Polyether polyurethanes could be synthesized with the desired properties by varying the initial composition, the type of ingredients and their molecular weights.

G. B. Wang and et.al. [22] used polycaprolactone diol (PCL) ($M_n=1250$) and 2,4-toluene diisocyanate (TDI) to study the biological degradation products of biomaterials by High Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS). The reverse-phase HPLC separated more than twenty products associated with polyurethanes biodegradation. As well, double focusing MS analysis first scan filtered the ions fragmented from the samples and impurity ions from the mobile phase and allowed for the analysis in the second scan. No toluene-diamine – (a suspected human carcinogen associated with some medical implants) – could be found in the test samples.

Mutsuhisa Furukawa and et.al. [6] synthesized polyurethane elastomers with alkyl side group from 4,4'-diphenylmethane diisocyanate (MDI), poly (1,5-pentamethylene adipate)-glycol and 1,4-butanediol. They found that these polyurethanes have good mechanical properties comparable to those of the general purpose (hydrolytic stability) polyester urethanes and the introduction of methyl and ethyl side groups to the polymer chains enhanced the hydrolytic stability of the resulting polyurethanes.

Ten-Chin Wen and et.al. [30] used polyaddition of poly(propyleneglycol) (PPG) and dimethylol propionic acid (DMPA) with various diisocyanates for preparation of waterborne polyurethanes (WPU). Characterization of these polyurethanes carried out using Differential Scanning Calorimetry, Fourier Transform Infra Red Spectroscopy and Impedance Spectroscopy (IS) to monitor the phase change the conductivity of the polymers with the doped lithium perchlorate (LiClO_4). The T_g increased with increase in the added salt due to increased solution of the lithium cation with the oxygen of soft-segment ether linkage by formation of transient cross-links and the phase separation of aromatic diisocyanate-based WPUs is more significant than that of aliphatic ones in the addition of salts. The conductivity of WPU based electrolytes increased or decreased with increasing salt concentration as added salt level was unsaturated or saturated, respectively.

Kuo-Yu Chen and et.al. [34] used a hydroxy-terminated polytetramethyl oxide (PTMO) ($M_n=1000$), hexamethylene diisocyanate (HDI) with fluorinated 1,6-hexandiol and fluorinated 1,4-butanediol for preparation of fluorinated aliphatic polyurethanes. They found that the introduction of bulky fluorocarbon chains into the hard segments of polyurethanes had a large effect on the physical properties of these polymers and the longer CF_2 unit enhanced the effect. The bulky fluorocarbon chains might have a large influence on the hard segment packing of HDI since it is more structurally regular

compared to MDI. As well, higher fluorocarbon chain content significantly reduces the degree of platelet adhesion and platelet activation on the polyurethane surface.

Ling Hong and et.al. [14] synthesized a novel one-pot approach hyperbranched polyurethanes (HPs) from AB_n macromonomers containing linear units to study their properties. Characterizations were carried out using ^1H NMR, ^{13}C NMR, Fourier Transform Infra Red Spectroscopy, Gel Permeation Chromatography and Thermogravimetric Analysis. They concluded that the ionic conductivity of these HPs was affected by the salt concentration (LiClO_4), the concentration of HP and the chain length of ethylene glycol. The conductivity increased as the added HPs increased. Furthermore, the conductivity could be enhanced by longer ethylene glycol chains and higher concentrations of LiClO_4 in the HP materials.

Katarzyna Gorna and et.al. [23] used aliphatic hexamethylene diisocyanate (HMDI), isophorone diisocyanate (IPDI), polycaprolactone diols (PCL; 530, 1250 and 2000) with 1,4-butanediol (BD) and other chain extenders to synthesize biodegradable poly(ϵ -caprolactone urethane)s for studying the effect of the polyol molecular weight, catalyst and chain extenders on the molecular and physical properties. The T_g 's for the produced polyurethanes ranged from -57 to -38°C and were higher for polymers based on isophorone diisocyanate with higher hard segment contents. They found that there was little effect from molecular weight on the thermal properties. The tensile strength and tensile moduli were increased with increasing hard segment content, which increase phase separation. The least effective catalyst was magnesium methoxide while the most effective one was ferric acetyl acetate due to higher reaction temperature and reaction mixture viscosity far at the end of the investigation period.

Anna Kultys and et.al. [27] synthesized thiopolyurethanes from thiodiols, hexamethylene diisocyanate and poly(oxytetramethylene) glycol (PTMG) by a one-pot

melt polymerization. The structures of polyurethanes were determined by Fourier Transform Infrared Spectroscopy and X-ray Diffraction Analysis. The thermal properties were examined using Differential Scanning Calorimetry and Thermogravimetric Analysis. They concluded that all polyurethanes showed partially crystalline structures and increasing the PTMG content decreased hardness, modulus of elasticity and tensile strength. The elongation at break increased due to the higher molecular weight. The T_g 's were between -70°C and -59°C which were nearly independent of the hard segment content indicating a good microphase separation between hard and soft segments.

B. K. Kendagannaswamy and et.al. [28] used castor oil, 4,4'-diaminophenyl sulphone as chain extender and different diisocyanates to prepare chain-extended polyurethanes. The effect of aromatic diamines on the swelling and thermal degradation of the PU were examined. Thermogravimetric Analyzer (TGA) showed that thermal degradation of the polymers started at 194°C due to the complicated chemical structure. In addition the SEM photographs showed a two-phase morphology. The average molecular weight was determined by swelling studies.

Bor-Sen Chiou and et.al. [19] prepared polyurethanes from poly(propylene glycol), trimethylpropane propoxylate (triol) and 2,4-toluene diisocyanate (TDI). The crosslink density was controlled by varying the triol concentration from 10 to 70 mol % and the isocyanate-to-hydroxyl (NCO/OH) ratio from 1.0 to 1.3. They found that all samples had one glass transition temperature which increases more over the range of triol concentration studied than over the range of NCO/OH studied. No crystalline regions were detected. Samples with higher crosslink densities had much larger elastic moduli for temperatures above the T_g .

Stefan Operea and et.al. [29] used 4,4'-diphenylmethane diisocyanate (MDI) with poly (ester)diols for the preparation of poly(ester-urethane-methacrylate)s using a two-

step process: synthesis of an isocyanate terminated prepolymer and the reaction product with hexamethylenediamine followed by neutralization with methacrylic acid. They found that these polymers exhibited physical properties similar to those of linear segmented polyurethanes. The soft segment crystallinity increased as the polyester segment molecular weight increased and longer chain lengths between crosslinks produced higher elongations at break and lower mechanical moduli. The curing process increases the urethane acrylate domain rigidity and decreases the soft segment crystallinity, which enhances the tensile strength of the cured materials.

Most of the polymerization processes carried out in the above studies were solution polymerization in which solvent, catalysts and other additives were added to the reaction pots. In this study, the polymerization was carried out in bulk with no need for solvent and other additives which make quite attractive process from industrial point of view.

2.3. Polyurethane Chemistry:

Polyurethanes are among the most widely used and versatile of all polymers, ranging from soft elastomers, adhesives and foams, to hard plastics [35]. Table 2.1 presents recognized names of the two important linkages found in polymers, comparing classical organic chemistry nomenclature to that used in polymer chemistry and biochemistry. They are manufactured from many different starting materials and a broad range of additives [10]. This part aims at highlighting the chemistry of polyurethanes.

Polyurethanes are a family of heterogeneous polymers; they contain the urethane linkage within the polymer chains and have the ability to incorporate other functional groups into the polymer network that contribute to the broad range of properties exhibited by polyurethane materials. These properties range from rigid hard thermosetting materials to those of much softer elastomers. In general, thermoplastic polyurethanes, which comprise the most important group for implantable devices, have very high tensile

strength, toughness, abrasion resistance, and resistance to degradation, in addition to biocompatibility that has sustained their use as biomaterials [40].

Table 2.1: Recognized Nomenclature of some important Polymers.

Linkage	Organic Chemistry	Polymer Chemistry	Biochemistry
$\begin{array}{c} \text{H} \quad \text{O} \\ \quad \\ \text{---N---C---} \end{array}$	Amide	Nylon	Peptide
$\begin{array}{c} \text{H} \quad \text{O} \\ \quad \\ \text{---N---C---O---} \end{array}$	Carbamate	Urethane	Not applicable

The chemistry of polyurethanes starts with the reaction of an isocyanate with a hydroxyl group. Additives to polyurethanes include catalysts, blowing agents, surfactants, pigments, fillers, flame-retardants and antigradants. These vary from water to heavy metal compounds.

The high reactivity of isocyanate toward nucleophilic reagents is mainly due to the pronounced positive character of the C-atom in the cumulative double bond sequence consisting of nitrogen, carbon and oxygen, especially in aromatic systems . The electronic structure of the isocyanate group can be represented by several resonance structures, which are illustrated in figure 2.1.

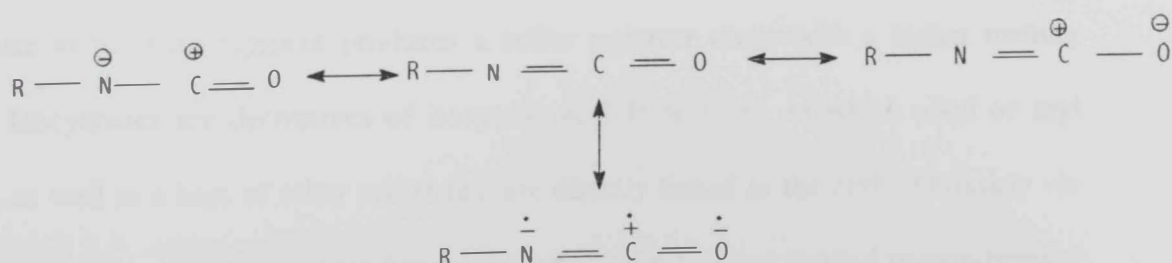


Figure 2.1: Resonance structure of the isocyanate group.

From the resonance structures, the positive charge at the C-atom becomes obvious. On the other hand, the negative charge can be delocalized onto the oxygen atom, nitrogen atom, and the R group, if R is an aromatic group. This explains why an aromatic isocyanate has a distinctly higher reactivity over an aliphatic isocyanate [40]. Furthermore, the substituents on the aromatic ring can also influence the positive character of the NCO group: an electron withdrawing group in the para or ortho position.

The electron distribution of the isocyanate group means that the species can react with either electron donors or electron acceptors. But most reactions of isocyanates involve addition to the N=C double bond. Aromatic isocyanates are generally more reactive than aliphatic ones as the electron withdrawing nature of the benzene ring makes the isocyanate carbon more susceptible to nucleophilic attack. Electron donating substituents near the isocyanate carbon will reduce the rate of reaction of the isocyanate. The presence of bulky side groups in the ortho- position of aromatic isocyanates, or branched or bulky substituents on aliphatic molecules will sterically hinder the approach of electron donors, and reduce the rate of reaction [40].

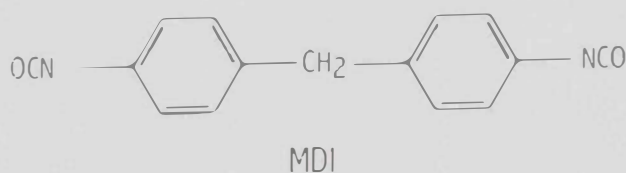
2.3.1 Raw materials in Polyurethane synthesis:

2.3.1.1. Isocyanates:

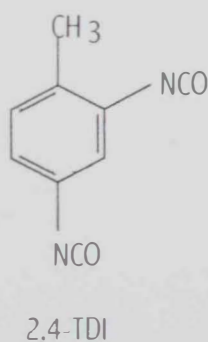
Both aliphatic and aromatic isocyanates can be used to synthesize polyurethanes. The most widely used diisocyanates are shown in table 1.2. The presence of an aromatic isocyanate in the hard segment produces a stiffer polymer chain with a higher melting point. Isocyanates are derivatives of isocyanic acid $\text{H}-\text{N}=\text{C}=\text{O}$, in which alkyl or aryl groups, as well as a host of other substrates, are directly linked to the $\text{N}=\text{C}=\text{O}$ moiety via the nitrogen atom. The isocyanate functionality is highly reactive toward proton-bearing

nucleophiles. This reaction occurs by nucleophilic addition across the carbon nitrogen double bond [40].

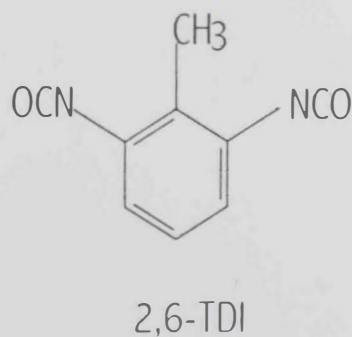
The two most commonly used isocyanates in polyurethane synthesis are methylene bis(*p*-phenyl isocyanate) or 4,4'- Diphenylmethane diisocyanate (MDI) as shown in scheme 2.1 and toluene diisocyanate TDI (an 80/20 mixture of 2,4- and 2,6-isomers) as shown in schemes 2.2 and 2.3. Both materials are derived from readily-available petrochemical intermediates and are manufactured by well understood and closely defined chemical processes [38]. TDI is less expensive than MDI, but MDI has superior reactivity and polymers based on MDI may possess better physical properties. MDI is crystallizable while TDI does not crystallize. MDI is a solid and has a functionality of 2.0 which makes it well suited for the preparation of high performance elastomers [13, 38]. The manufacturing process of MDI is considerably more complex than that of TDI as shown in figure 2.2 and figure 2.3.



Scheme 2.1: 4,4'- Diphenylmethane diisocyanate (MDI)



Scheme 2.2: 2,4- toluene diisocyanate



Scheme 2.3: 2,6- toluene diisocyanate

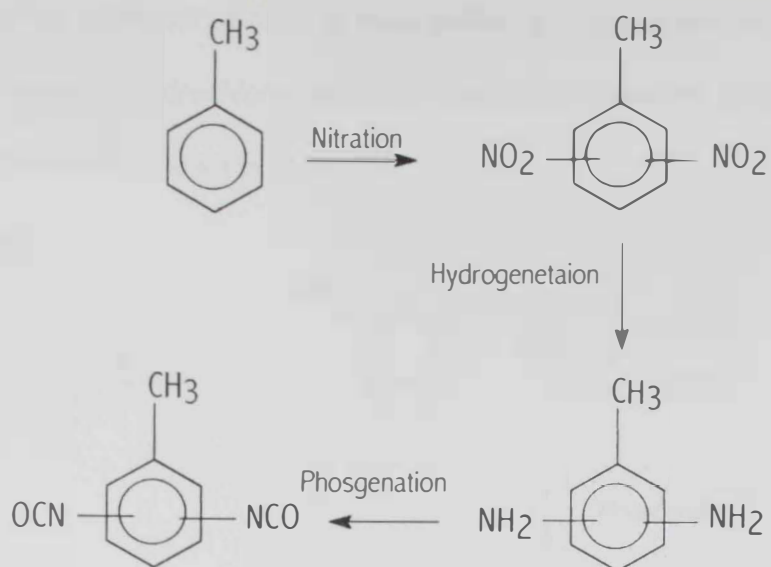


Figure 2.2: Synthesis of toluene diisocyanate

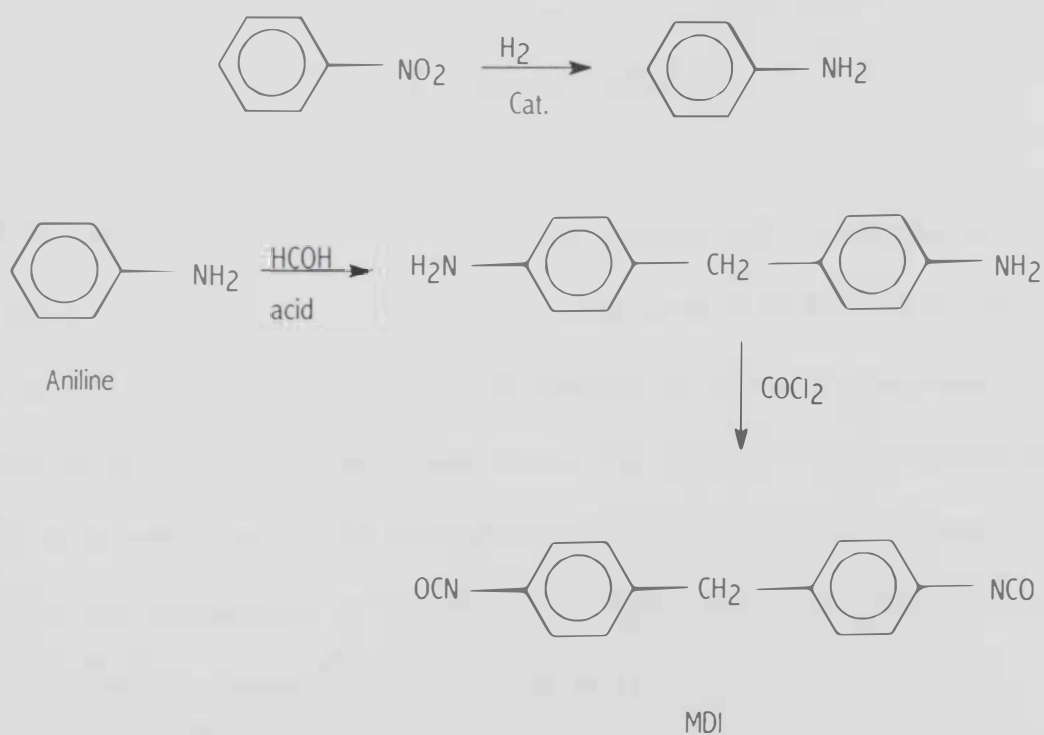


Figure 2.3: MDI manufacturing process [41].

Another method for synthesis of MDI is from aniline and formaldehyde, which react together in the presence of hydrochloric acid as a catalyst, followed by phosgenation of the corresponding diamine as shown in figure 2.4.

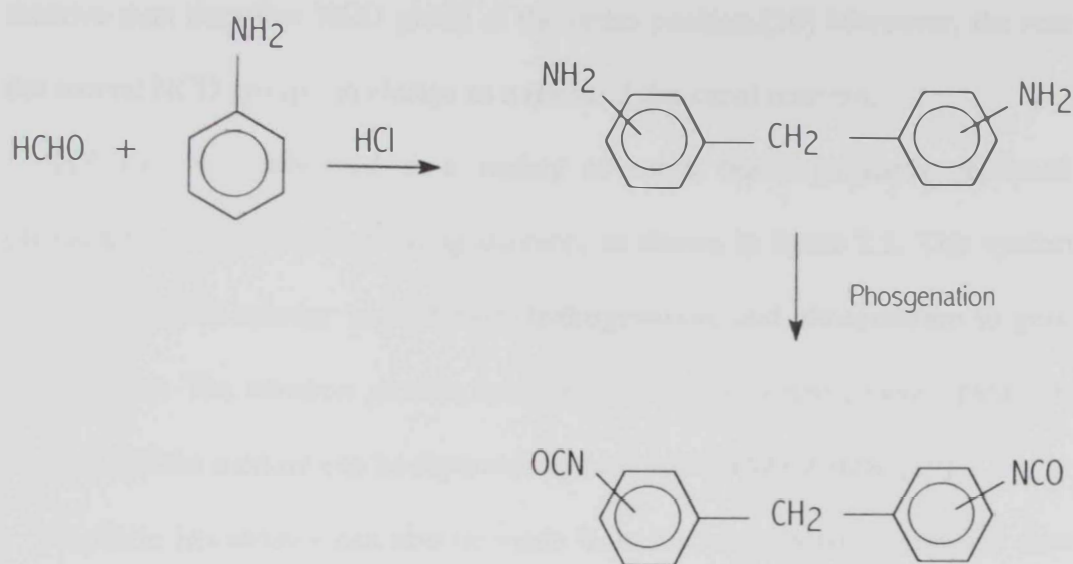


Figure 2.4: Synthesis of MDI [20].

MDI is a white to pale yellow solid at room temperature, with a molecular weight of 250.26 has a boiling point of $> 300^\circ\text{C}$ and a melting point of $39\text{--}43^\circ\text{C}$. It is soluble in octane, benzene and kerosene and used for the synthesis of various fibers and elastomers. MDI tends to form insoluble dimers when stored. The difficulty of handling solid pure MDI and its increased tendency to form a dimer when stored as a liquid at over 40°C , have led to the development of modified pure MDIs which are liquid at ordinary temperatures and have a reduced tendency to dimerise [42].

In general, aromatic isocyanates are more reactive than aliphatic isocyanates, which can only be utilized if their reactivities match the specific polymer reaction and special properties desired in the final product. For example, polyurethane coatings made from aliphatic isocyanates are photo-stable [43], while coatings made from an aromatic isocyanate do undergo photo-degradation.[44] Furthermore, the reactivity of an

isocyanate group can vary dramatically even for the same class of isocyanate. The structure, substituents, and steric effect can all influence reactivity. For example, in 2,4-toluene diisocyanate, the isocyanate group para to the methyl group is 25 times more reactive than the other NCO group at the ortho position.[20] Moreover, the reactivity of the second NCO group can change as a result of the initial reaction.

TDI can be synthesized in a variety of ways, but is primarily produced by the phosgenation of the corresponding diamine, as shown in figure 2.2. This synthetic route often starts with toluene via nitration, hydrogenation, and phosgenation to generate the diisocyanate. The nitration process leads to a mixture of ortho-, meta-, para-nitrotoluene isomers and the mixture can be separated by several distillation steps [20].

Aliphatic isocyanates can also be made from the corresponding aliphatic diamines via the phosgenation process. Cyclic aliphatic diamines are, in many cases, available through ring hydrogenation of the corresponding aromatic amines, such as the hydrogenation of diamino diphenyl methane (MDA) to give diamino dicyclohexyl methane. The most important aliphatic isocyanates are 1,6-hexamethylene diisocyanate (HDI), 1-isocyanato-3-isocyanatomethyl-3,5,5-trimethyl-cyclohexane (IPDI) and 4,4'-diisocyanato dicyclohexylmethane (HMDI). These aliphatic isocyanates, or their modified forms, are widely used in the coating industry [38].

2.3.1.2.Polyols:

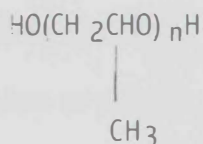
Polyols available for polyurethane synthesis include polyesters, polyethers, polycarbonates, hydrocarbons and polydimethylsiloxanes. The most commonly used polyols are polyether or polyester based compounds of molecular weight 400 – 5000 [16,40].

The structure of the polyol plays a large part in determining the properties of the final urethane polymer. The molecular weight and the functionality of the polyol are the main factors, but the structure of the polyol chains is also important.

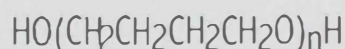
Polyether polyols: About 90 % of the polyols used in polyurethane manufacturing are hydroxyl-terminated polyethers.

These materials are the products of a reaction between a simple starter molecule such as ethylene glycol, propylene glycol, glycerin or sucrose with a cyclic ester such as ethylene oxide, propylene oxide, or tetrahydrofuran [38].

Polyether-based polyols produce very high quality polyurethane foams and elastomers. Among the most important polyether polyols are the polybutanediol, polypropylene oxide glycol (PPO) and polybutylene oxide glycol (PBO) as shown in schemes 2.4(a) and 2.4(b) respectively. Polyether urethanes have been found to degrade due to environmental stress cracking [41,45].



(a)



(b)

Scheme 2.4: (a) Polypropylene oxide glycol (PPO). (b) polybutylene oxide glycol (PBO)

Polyethylene oxide (PEO) based urethanes exhibit poor water resistance due to the hydrophilic nature of the ethylene oxide. Polypropylene oxide (PPO) has also been widely used because of its low cost and reasonable hydrolytic stability, although the mechanical properties of urethanes made from polypropylene oxide are not as good as those made from polytetramethylene oxide (PTMO) or polyester [46].

Among the polyether based polyurethane elastomers, the one made from the soft segment polytetramethyleneoxide (PTMO) exhibits the best mechanical properties which

are comparable to those of polyester polyurethanes. In addition, these polyurethanes show outstanding hydrolytic stability, good low temperature flexibility, good thermal stability, high fungus resistance, and excellent abrasion resistance [45].

When the application requires good environmental stability, a polydiene based soft segment is a good candidate. Hydrogenated polybutadiene and polyisobutylene based polyurethanes often show excellent resistance to photo degradation, thermal degradation, and hydrolysis.[47,48] However, the physical properties of these polyurethanes are poor compared to those of conventional polyurethanes. Furthermore, the synthesis of these materials is complicated, which can increase the cost. However, introduction of polydimethylsiloxane (PDMS) as a soft segment results in a polyurethane with improved low-temperature properties, since the glass transition temperature (T_g) of PDMS is around -123°C . Nonetheless; the physical properties of these urethanes are still not as good as those of conventional polyurethanes at room temperature [49].

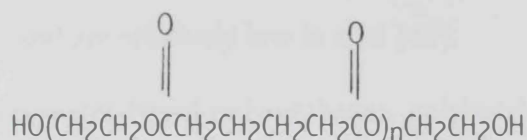
Polyester polyols: These are polyalkylene glycol esters such as polybutylene terphthalate or adipate. Saturated polyethers with terminated-hydroxyl groups are used to make both flexible and rigid polyurethane polymers. Polyester polyols tend to be more expensive than polyether polyols and they are usually more viscous and therefore more difficult to handle. Polyester urethanes contain a conjugated carbonate linkage (O-CO-O) in the soft segment which makes them more stable than the polyether urethanes that contain ether linkage (C-O-C) [38].

Polyester-based polyurethane elastomers combine high levels of tensile properties with resistance to flexing and abrasion. They also have good resistance to many types of oil. Polyesters are typically made by the condensation reaction between glycols and dicarboxylic acids. Branching can be introduced by the addition of a small amount of a

triol to the reaction mixture. As esterification proceeds the water produced is removed from the reaction [38].

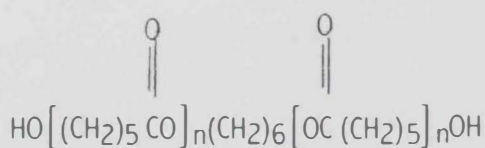
Polyester polyols for making polyurethanes include:

- (i) Scheme 2.5 shows poly (ethylene adipates), which are wax-like solids at room temperature and are mostly used in the manufacturing of polyurethane elastomers and adhesives.



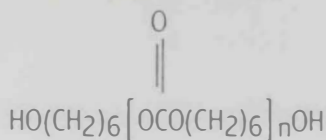
Scheme 2.5: Poly (ethylene adipates).

- (ii) Polycaprolactone diols as shown in scheme 2.6 have lower viscosities but are more expensive than polyadipates of similar molecular weight. Copolymer diols of Polycaprolactones and polyadipates are easy to handle because they are often liquids of relatively low viscosity at room temperature. Polycaprolactone diols give elastomers with relatively good resistance to hydrolysis but similar stability can be obtained with polyadipates by increasing the molecular weight of the glycols [38].



Scheme 2.6: Polycaprolactone diol.

Polycarbonates: such as poly(1,6-hexanediol)carbonate -in scheme 2.7- which is prepared by condensation of phosgene or alkylene glycol carbonates with alkylene glycols such as 1,6-hexanediol [41].



Scheme 2.7: poly (1,6-hexanediol)carbonate.

Traditionally, polyurethanes have been produced with polyester and polyether soft segments. Polyesters give the polyurethanes relatively good physical properties, and have very high tensile strength, very high tear strength, and are easy to prepare. They have excellent abrasion resistance and are relatively low in cost [40].

Figure 2.5 shows, two polyester-based polyurethanes, polybutylene adipate glycol and polyethylene adipate glycol, have retained only 40 and 18 percent of their respective initial strength when aged at high temperature and humidity for 3 weeks. A Polycaprolactone-based elastomer loses 50 percent of the initial tensile strength after 4.5 weeks. By contrast, the polyether-based polyurethane remains unchanged for the duration of the test. Polyethers exhibit a relatively high resistance to hydrolytic cleavage and are favored for use in applications where hydrolytic stability is required [10].

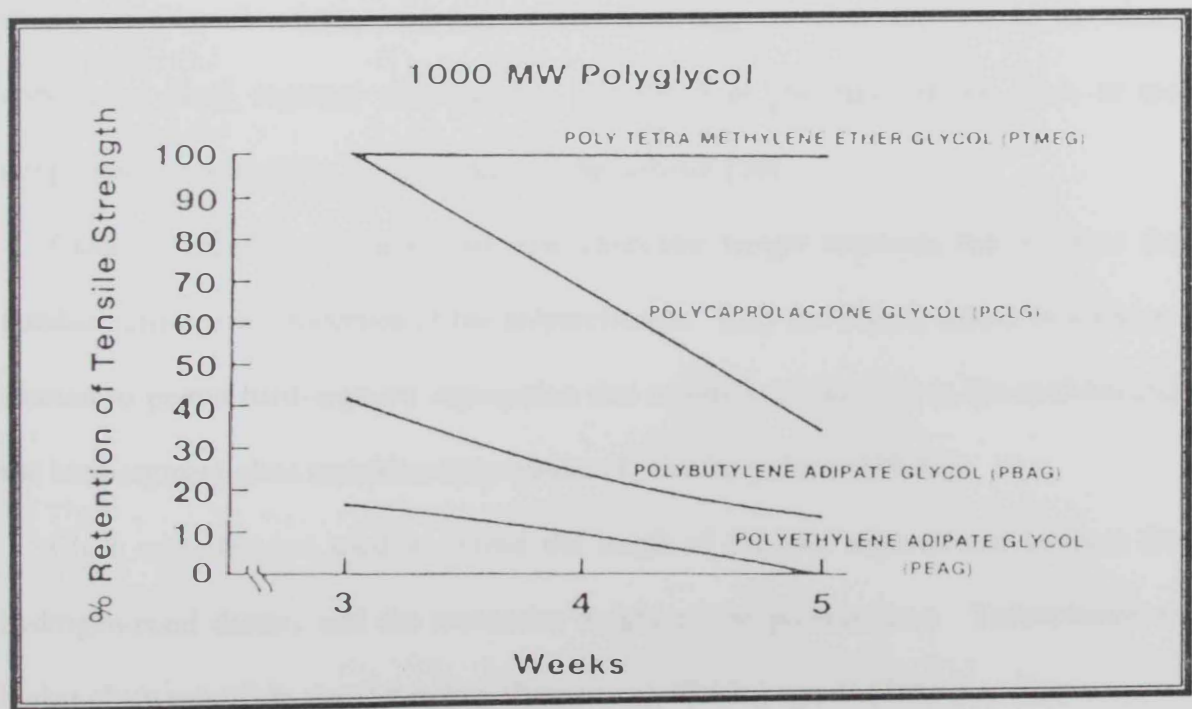


Figure 2.5: Polyurethane performance (MDI/BDO) humidity aging at 80°C / 95 % RH.

2.3.1.3 Chain extenders:

Apart from polyisocyanate and polyols, a wide variety of auxiliary chemicals may be added in order to control and modify both the polyurethane reaction itself and the properties of the final polymer. These additives include catalysts, cross-linking agents, chain-extending agents, blowing agents, surfactants, coloring materials, fillers, smoke suppressants and flame retardants [38].

In addition to polyol and diisocyanate, low molecular weight diol and diamine chain extenders play a very important role in polyurethanes as well. Without a chain extender, a polyurethane formed by directly reacting diisocyanate and polyol generally has very poor physical properties and often does not exhibit microphase separation. Thus, the introduction of a chain extender can increase the hard segment length to permit hard-segment segregation, which results in excellent mechanical properties, such as an increase in the modulus and an increase in the hard-segment glass transition temperature (T_g) of the polymer. By modifying the ratio between the polyol and chain extender, polyurethanes can change from a hard, brittle thermoplastic to a rubbery elastomer, simply as a result of the variation of the hard segment concentration in the block copolymer. Hard segment concentration is defined as the ratio of the mass of the nonpolyol components to the total mass of the polymer [50].

Chain extenders or curatives are low molecular weight reactants that produce the familiar elastomeric properties of the polyurethanes. They are usually added in sufficient amount to permit hard-segment segregation that results in an increase in the modulus and the hard-segment glass transition temperature (T_g) of the polymer [38,41].

Chain extenders are used to extend the length of the hard segment and increase the hydrogen-bond density and the molecular weight of the polyurethane. Trifunctional or higher chain extenders also act as branching or crosslinking agents [40].

Ethylene glycol and 1,4-butanediol have attained great commercial significance. 1,4-butanediol is the most important chain extender in elastomeric systems.

To synthesize thermoplastic polyurethanes, the chain extenders must be linear diols. If a branched diol is used, crosslinking occurs, and the polymer is no longer capable of being processed by thermal methods. Of the available chain extenders, 1,4-butanediol is the universal choice for medical applications. This chain extender produces thermoplastic polyurethanes with high physical properties, excellent processing conditions and clear polymers. Butanediol- extended polyurethanes display the best combination of physical properties and hardness as presented in table 2.2 [10].

Table 2.2: Physical properties of polyurethane elastomers as influenced by glycols.

Glycol	Tensile (PSI)	Elongation (%)	Modulus (PSI)	Tear (LB/IN)	Hardness (Shore B)
Ethylene	6500	500	2000	230	61
1,3-Propanediol	6600	600	950	270	61
1,4-Butanediol	7900	600	1000	270	61
1,6-Hexanediol	7400	500	850	170	60
1,5-Pentandiol	7100	600	900	280	62

Amine-containing chain extenders generally react more rapidly than the corresponding hydroxyl-containing materials and these amine-containing chain extenders may impart an odor to the resultant polymeric product.

They give properties superior to those of similar polymers prepared with the equivalent diol chain extender. This is because the hard segment (urea linkage) has a higher density of hydrogen bonding, which results in a higher T_g and higher thermal stability. However, for the same reason, polyurethane ureas made from diamine chain

extenders tend to be less soluble in common solvents and are thus more difficult to melt. In addition, due to electron delocalization, the aromatic chain extenders have less reactivity than aliphatic chain extenders, which could be favorable in reactions that need to be highly controlled [51].

The reaction between a polyol and a polyisocyanate produces a polyurethane, while the reaction between a polyamine and a polyisocyanate produces a polyurea, and a reaction involving a polyol, a polyisocyanate and a polyamine chain extender produces a poly(urethane/urea) [41].

Noncrosslinked polyurethanes are synthesized using linear dihydroxy polyester or polyether compounds and excess diisocyanate to form the prepolymer which is then reacted with the chain extender in exact molar proportions calculated from the free isocyanate present. The resulting polymer can be dissolved in polar solvents such as tetrahydrofuran (THF) and dimethylformamide (DMF) [40].

To prepare crosslinked polyurethanes, an excess of isocyanate must be used in the chain extension step, allowing heat-curing side reactions to occur.

The properties of the produced polyurethanes depend on the length and structure of the segments, the stoichiometric ratio of the components, and the degree of branching. For optimal mechanical strength, the ratio of isocyanate groups to hydroxy groups should be 1.0 – 1.1. If it is less than 1.0, the molecular weight, mechanical strength and the hardness of the material decreases [40].

2.4 Structure-Property Relationship in Polyurethanes:

2.4.1. General principles:

In most polymers when molecules are arranged in completely random, intertwined coils, the un-ordered structure is known as the amorphous state. When the molecules are so neatly arranged that each atom falls into a precise position in a tightly packed repeating

regular structure, this highly oriented structure is described as the crystalline state. Polyurethane elastomer structures are two-phase structures, where the hard segments separate to form discrete domains in a matrix of soft segments. This arrangement is termed segmented and thus polyurethane elastomers are segmented polymers. The glass transition temperature of one of the segments is well below the ambient ($\sim -40^{\circ}\text{C}$) and is therefore considered to be a rubbery or 'soft' segment, whereas the glass transition temperature of the other segment is well above the ambient ($\sim 50^{\circ}\text{C}$) and is therefore considered to be a rigid or 'hard' segment. The rigid segments act as bridges, and as filler particles, reinforcing the soft segment matrix [10].

Polyurethanes are segmented or block copolymers, consisting of alternating hard segments that are formed by a diisocyanate and a chain extender (which may be glassy or semicrystalline) and soft segments which are composed of a polyol (elastomeric). The microphase separation of these two chemically distinct components gives rise to the useful physical and mechanical properties of polyurethanes. The driving force behind the phase separation into hard and soft domains is the chemical incompatibility of the hard and soft segments [52]. The hard segments consist of urethane segments and form glassy or semicrystalline domains, while the soft segments form an amorphous or semicrystalline matrix in which the hard segments are dispersed at low-to-moderate hard segment content. These hard domains act as multifunctional crosslinking sites and reinforcing fillers, resulting in materials which possess high modulus and exhibit elastomeric behavior [52,53].

At low temperatures, the glass transition temperature (T_g) of the soft segment influence the mechanical properties of the polymer, while at higher temperatures, either the glass transition or the melting (T_m) of the hard segment determines the point at which the physical crosslinks dissociate.

The general principles of the structure-property relationship can be summarized as follows:

Molecular weight : As the molecular weight increases some properties such as tensile strength, melting, elongation, glass transition temperature, etc. increase up to a limiting value.

Intermolecular forces: Weaker secondary bonds such as hydrogen bonding, dipole interactions and Van der Waals forces may form, in addition to the primary chemical bonds and these bonds are affected by temperature and stress. If there is extensive cross-linking, the role that intermolecular forces play is reduced.

Stiffness of chains: Presence of aromatic rings stiffens the polymer chain and increases melting point, increases hardness and decreases elasticity. While the presence of flexible bonds favors softness, low melting, low glass transition temperature, and elasticity.

Crystallization: Linearity and close fitness of polymer chains favor crystallinity, which leads to reduction in solubility, elasticity, elongation, flexibility and increases tensile strength, melting point and hardness.

Cross-linking: An increase in the degree of cross-linking causes an increase in rigidity, softening point, and modulus of elasticity for amorphous polymers, and reduces elongation and swelling by solvents [41].

Figure 2.6 presents a summary of structure-property relationship for polyurethanes; branching/crosslinking is plotted on the ordinate, and intermolecular forces on the abscissa. Under these conditions, it is feasible to encompass all the commercially available polyurethanes, and define which elastomeric products are of greatest importance in biomedical applications. At the extreme (the right corner), the thermoset rigid foams occupy the highest rank of crosslinking and chain stiffness [10].

None of the polyurethanes listed at either extreme of figure 2.6 have attained any sort of clinical significance. The same can be said about flexible foams, semi-rigid foams, and microcellular foams. Thin thermoplastic polyurethane films are widely used in semi-occlusive wound dressings, and a cast thermoset elastomer has been used for many years with success. However, none of these are implantable grade polymers [10].

At about 180°C, aromatic polyurethanes start to revert. For aliphatic polyurethanes, this reversion takes place at around 160°C. And at temperatures above 250°C, all polyurethanes start to decompose giving rise to free isocyanates, alcohols, free amines, olefins, and carbon dioxide [41].

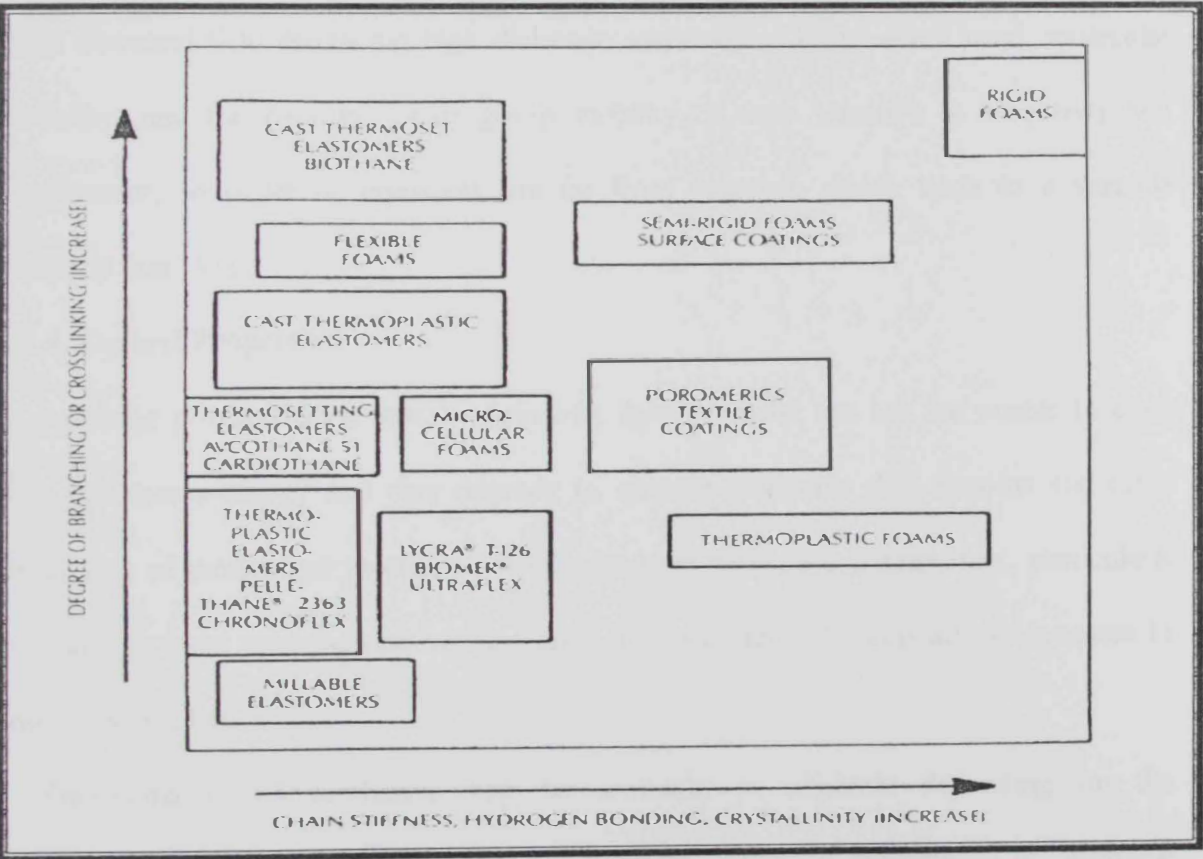


Figure 2.6: Structure-Property relationships in polyurethanes.

2.4.2. Thermal Properties:

Thermal properties of polyurethanes depend primarily on the polymerization \rightleftharpoons depolymerization equilibria of the functional groups in the polymer molecule. Conventional urethane and urea links decompose at considerably high temperatures but Isocyanurate rings are more stable than urethane and urea links. Flammability of polyurethane is a frequent concern, especially when it comes to soft polyurethanes used in furnishing and bedding materials [41].

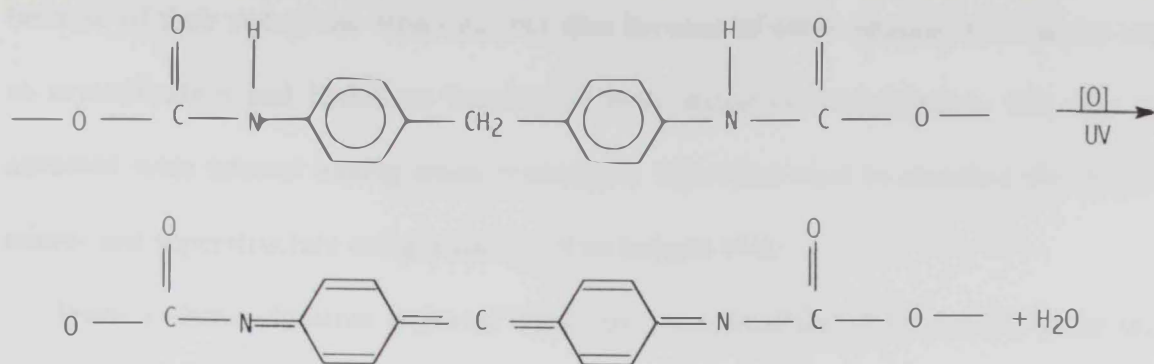
2.4.3. Electrical Properties:

Polyurethanes contain many polar groups that tend to orient in an electrical field, and most polyurethane molecules have enough flexibility to permit their polar groups to orient in an electrical field producing high dielectric constants. On the other hand, molecular flexibility, and the resulting polar group mobility, is very sensitive to frequency and temperature, so dielectric constants are far from constant, which leads to a variable dielectric loss [41].

2.4.4. Optical Properties:

Aromatic polyurethanes absorb ultraviolet light from the sun but are unable to cope with the excess energy and they degrade to quinoid structures that discolor and often suffer loss of mechanical properties. Where weather resistance is important, particularly in coatings, most manufactures replace aromatic isocyanates by aliphatic isocyanates to solve this problem [41].

Thermoplastic polyurethanes may be aromatic or aliphatic depending on the isocyanate source that is used in the synthesis. One disadvantage of aromatic polyurethanes is that polymers based on aromatic isocyanates will turn yellow upon exposure to ultraviolet radiation. The chemical equation that shows the basic fundamental principle of how these materials turn yellow is shown in figure 2.7.



Di-quinone-imide (chromophoric)

Figure 2.7: Quinoid structure of aromatic isocyanate.

Figure 2.7 shows MDI, which has been reacted with a hydroxyl group to form an NH-CO-O group, a urethane linkage on either side of the aromatic group [10].

Under the influence of UV light and oxygen, there is molecular rearrangement where the methylene group that is between the two benzene groups loses its hydrogens. The nitrogen also loses its hydrogen, forming water by combining with atmospheric oxygen, and a di-quinone imide structure is formed. The di-quinone imide structure is a chromophoric group that absorbs all colors except yellow. Therefore, aromatic polyurethane, when exposed to UV radiation (say from fluorescent light), tends to get more yellow with the passage of time.

Aliphatic polyurethanes, on the other hand, do not show the embrittlement, weakening and progressive darkening of the aromatic-based polyurethanes. This led to the search for nonyellowing isocyanate sources [10].

It is evident that the morphology of a multiphase system plays an important role in determining the final properties of the polymers. By controlled variation of the morphology, the desired properties can be obtained for a material. Hence, a profound knowledge of morphology is essential to understanding structure-property relationships. Unfortunately, the morphology of segmented polyurethanes is very complicated, not only

because of their two-phase structure, but also because of other physical phenomena such as crystallization and hydrogen bonding in both segments. Nevertheless, this area has attracted wide interest among many researchers who have tried to elucidate the detailed micro- and superstructure using a variety of techniques [54].

From a thermodynamic point of view, the incompatibility between the polar hard segment and less polar soft segment in the polyurethane causes the heat of mixing to be positive and drives the two segments to phase separate. The degree of phase segregation between the hard and soft segments depends on molecular weight and the interaction of hard segments with each other and with the soft segments. For example, phase segregation is more pronounced in polybutadiene urethanes than in polyether urethanes, and is least evident in polyester urethanes. Moreover, the interaction between the hard segments depends on the symmetry of the diisocyanate and on the selection of the chain extender (diol or diamine). A diisocyanate and a chain extender having a more symmetrical structure will enhance the formation of organized structures, and thus, more complete phase segregation. A urea-containing hard segment formed from low molecular weight diamine chain extender has a much more pronounced phase separation than urethane- containing hard segments because of the higher polarity of the urea hard segment [55].

The morphology of segmented polyurethanes can be studied at three different structural levels according to their size. The smallest structural level is the molecular structure such as crystal structure, block sequence and sequence distribution, which can be investigated by NMR and IR spectroscopy. The second level of structure is domain structure, which has the dimension of 50-1000 Å [20]. A complete description of sample morphology at this level consists of the determination of the phase volume fraction, size, shape, orientation, connectivity, and interfacial thickness as a function of segment content

and sample history [50]. This structural level can be directly probed by electron microscopy, or more quantitatively by Small Angle X-ray Scattering. The third level of morphology is spherulitic texture and when size considerations are in the micron range. This type of morphology can be investigated using small angle light scattering, electron microscopy and polarized light microscopy. These methods can be complemented by thermal analysis methods such as differential scanning calorimetry and dynamic mechanical analysis to render additional, if somewhat less direct, information on the domain structure.

The mobility of the polyol results in low-temperature properties and the variation in ultimate stress values in the segmented polyurethane. Therefore, it is obvious that features related to the mobility of the polyols such as T_g , T_m , and the ability to crystallize under deformation, will certainly impact mechanical properties. It has also been reported that stress induced crystallization can improve tear resistance and tensile strength, while at the same time diminishing recovery characteristics [56-58]. Polyol mobility depends to a large extent on the type and the molecular weight of the polyol. To prepare products with typical rubber elasticity, an average molecular weight of between 1000 and 4000 (which corresponds to a chain length of 180 and 300 Å) is desirable [20]. Higher molecular weight polyols afford materials with better tensile properties but with an increased tendency to cold-harden, which is a phenomenon caused by gradual crystallization of the flexible blocks during storage. This can be avoided by incorporating copolyester to provide structure irregularity [46]. In general, the primary consequences of increasing the molecular weight of the soft block for a given overall molar ratio of polyol block to hard block (diisocyanate plus chain extender) are, a decrease in modulus and an increase in elongation at break.

Polyethers usually have a lower T_g and a weaker interchain force than polyesters, thus polyethers generally render the corresponding polyurethanes with reduced mechanical properties. This is often attributed to the stronger hydrogen bonding between the NH and the ester carbonyl group, rather than urethane NH-ether oxygen bond. Among polyethers, Poly(tetramethylene glycol) based polyurethane has the best physical properties, which is a reflection of the regularity of its chain structure and its ability to crystallize upon extension [46]. On the other hand, the atactic side chain methyl group in poly(propylene glycol) prevents crystallization, resulting in weaker mechanical properties.

The effect of a chain extender on material properties depends on the type of chain extender used. When diamine is used as chain extender, better physical properties usually result than if a diol was used, due to stronger interchain interaction from the urea linkage.

Schollenberger has investigated the effect of different diols on polyurethane properties. One polyol that was employed was poly(tetramethylene adipate)glycol ($M_n=1000$) with MDI as diisocyanate. A constant mole ratio of (1:2:1) of polyol to diisocyanate to diol was used. The results showed that the mechanical properties resulting from this study were all excellent. However, the aliphatic glycol containing aromatic structure demonstrated the highest modulus and hardness [59].

The structure of the diisocyanates has a profound effect on high temperature properties. Factors such as high symmetry and rigidity in the p-phenylene diisocyanate lead to high modulus and excellent tensile strength. Reducing the bulkiness of the diisocyanate from naphthalene to 1,4-phenylene results in a drop in modulus. Moreover, the effect of the methyl group is remarkable and results in a large drop in modulus. This is shown in comparison of 4,4'-diphenylmethane diisocyanate and 3,3'-dimethyl-4,4'-diphenylmethane diisocyanate, on the one hand, and the 2,4-toluene diisocyanate and 1,4-

phenylene diisocyanate on the other. This is due to the fact that the methyl substituent can seriously disrupt the symmetry and crystallizability of the diisocyanates.

Nevertheless, the symmetry of MDI is sufficient to allow the preparation of a semicrystalline hard block, which is reflected by its excellent tensile strength. Aliphatic, e.g. hexamethylene diisocyanate, or cycloaliphatic diisocyanates, e.g. hydrogenated MDI, can offer better light stability over the aromatic isocyanate. They also show increased phase separation behavior over the corresponding aromatic diisocyanates. Another important feature of the aliphatic diisocyanates is transparency, which also arises from the presence of geometric isomers in these diisocyanates. H₁₂ MDI and IPDI are now well established as being preferred for the production of transparent weatherable polyurethane elastomers [46].

2.5. Polyurethanes in medical applications

2.5.1. Biomaterials:

In the treatment of many human diseases, it may be required to replace a diseased organ or do such procedures which involve the use of materials foreign to the body; these materials, are known as biomaterials [53]. Biomaterials are substances contained in therapeutic or diagnostic systems that are in contact with tissue or biological fluids. Therefore, they are defined as a nonviable material used in medical devices, intended to interact with biological systems [40].

2.5.2. Biomaterials applications:

Among the prominent applications for biomaterials are:

- ❖ Orthopedics—joint replacements (hip, knee), bone cements, bone defect fillers, fracture fixation plates, and artificial tendons and ligaments.

- ❖ Cardiovascular—vascular grafts, heart valves, pacemakers, artificial heart and ventricular assist device components, balloons, and blood substitutes.
- ❖ Ophthalmics—contact lenses, corneal implants and artificial corneas, and intraocular lenses.
- ❖ Other applications—dental implants, cochlear implants, tissue screws and tacks, burn and wound dressings and artificial skin, tissue adhesives and sealants, drug-delivery systems, matrices for cell encapsulation and tissue engineering, and sutures.

The types of materials featured in the above uses include metals (stainless steel, titanium and cobalt chrome), ceramics and glasses (alumina, calcium phosphate, hydroxyapatite), and a wide range of synthetic and natural polymers [46].

A brief overview of some of the more exciting and recent developments that are radically expanding the capabilities of polymeric biomaterials is given below. These include:

- New approaches to biodegradable polymers.
- "Combinatorial" and "supramolecular" chemistry.
- So-called intelligent materials.
- Other new formulations, including phospholipids, polymers for gene therapy, enhanced polyurethanes, and protein-based polymers.

Some polymers with their medical applications are shown in table 2.3

Table 2.3: Biopolymers and their medical applications:

Polymer	Applications	Polymer	Applications
PDMS	Catheters and heart valves	Polytetrafluoroethylene	Heart valves, Vascular grafts and Nerve repair
Polyurethane	Ventricular assist devices	Polyethylene	Catheters and hip prosthesis
		Polymethylmethacrylate (PMMA)	Fracture fixation
PGA, PLA and PLGA	Drug delivery devices	Cellophane	Dialysis membranes

2.5.3. Biomaterials properties:

Biomaterials should posses mechanical strength, a functional characteristic (the material has the specific property to perform the required task) and biocompatibility. Nevertheless, applications of biomaterials are limited by biocompatibility, the problem of adverse interactions arising at the junction between the biomaterial and the host tissue. The design or selection of a specific biomaterial depends on the relative importance of the various properties that are required for the intended medical application [60,61]. Physical properties that are generally considered include hardness, tensile strength, modulus, and elongation; fatigue strength, which is determined by a material's response to cyclic loads or strains; impact properties; resistance to abrasion and wear; long-term dimensional stability, which is described by a material's viscoelastic properties; swelling in aqueous media; and permeability to gases, water, and small biomolecules.

Poor selection of materials can lead to clinical problems. Teflon for example as biomaterial is noted for its low coefficient of friction and its chemical inertness but has relatively poor abrasion resistance. Thus, as an occluder in a heart valve or as an acetabular cup in hip-joint prosthesis, Teflon may eventually wear to such an extent that the device would fail [60]. The biocompatibility of a medical implant is influenced by a number of factors, including the toxicity of materials used, the form and design of the implant, the skill of the surgeon inserting the device, the dynamics or movement of the device in situ, the resistance of the device to chemical or structural degradation (biostability), and the nature of the reactions that occur at the biological interface.

2.5.4. Biodegradable Polymers:

As for other biomaterials, the basic design criteria for polymers used in the body call for compounds that are biocompatible (new definition), processable, sterilizable, and capable of controlled stability or degradation in response to biological conditions. The reasons for designing an implant that degrades over time often go beyond the obvious desire to eliminate the need for retrieval. For example, the very strength of a rigid metallic implant used in bone fixation can lead to problems with "stress shielding," whereas a bioabsorbable implant can increase ultimate bone strength by slowly transferring load to the bone as it heals. For drug delivery, the specific properties of various degradable systems can be precisely tailored to achieve optimal release kinetics of the drug or active agent [46]. An ideal biodegradable polymer for medical applications would have adequate mechanical properties to match the application (strong enough but not too strong), would not induce inflammation or other toxic response, would be fully metabolized once it degrades, and would be sterilizable and easily processed into a final end product with an acceptable shelf life. In general, polymer degradation is accelerated by greater hydrophilicity in the backbone or end groups, greater reactivity among

hydrolytic groups in the backbone, less crystallinity, greater porosity, and smaller finished device size.

Beginning in the 1960s, a range of synthetic biodegradable polymers have been developed, including polylactide (PLA), polyglycolide (PGA), poly(lactide-co-glycolide) (PLGA), polydioxanone, polyanhydride, trimethylene carbonate, poly(β -hydroxybutyrate), poly(γ -ethyl glutamate), poly(DTH iminocarbonate), poly(bisphenol A iminocarbonate), poly(ortho ester), polycyanoacrylate, and polyphosphazene. There are also a number of biodegradable polymers derived from natural sources such as modified polysaccharides (cellulose, chitin, dextran) or modified proteins (fibrin, casein) [48].

To date, the compounds that have been employed most widely in commercial applications are PGA and PLA, followed by PLGA, polydioxanone, trimethylene carbonate, and polyanhydride. Some of the common PLA products include tissue screws, tacks, and suture anchors, as well as systems for meniscus and cartilage repair.

2.5.5. Examples of biopolymers and their medical applications:

Many common thermoplastics, such as polyethylene, polyester and polyurethanes, are used as biomaterials. Thermoplastics usually exhibit moderate to high tensile strength (50 to 10,000 atmospheres of pressure) with moderate elongation (2 to 100%), and they undergo plastic deformation at high strains. Thermoplastics consist of linear or branched polymer chains; consequently, most can undergo reversible melt-solid transformation on heating, which allows for relatively easy processing or reprocessing [60].

2.5.5.1. Cellophane:

Often used in every day life to package products or to keep food fresh, cellophane is one of the most critical materials for the treatment of many kidney malfunctions.

Cellophane is regenerated cellulose. It is in the form of a film; as opposed to rayon, which has the same properties yet is a fiber. Cellophane holds almost identical properties to the naturally occurring cellulose, it is “regenerated” for processing purposes. It has a typical chain length ranging from 2000 – 6000 angstroms (longer in fibers) and a molecular weight varying widely from 300,000 to one million g/mol [62].

In 1959 Dr. Willem J. Kolff’s first artificial kidney was installed in St. Paul’s hospital in London. Ethical debate would continue for the next two years, but in 1961 the first dialysis was performed. Within 5 years a separate unit was opened in the hospital to treat patients suffering from renal problems. This machine used the idea of countercurrent flow, osmosis and diffusion to remove waste products from the blood stream, which are normally removed by the kidneys [63].

2.5.5.2. PGA, PLA, and PLGA:

The polymer polyglycolic acid, PGA, initially started out as an absorbable suture named Dexon. Dupont, under the direction of Norton Higgins, first synthesized PGA by a three-step process from glycolic acid by manipulating temperature and pressure. The ability of PGA to form biodegradable sutures, however, wasn’t found until 1963 by Edward Schmitt and Rocco Polistina of the American Cyanamid Corporation. Since the birth of PGA, derivatives of this polymer have been found to have useful medical properties as well.

Modifying the chemical and structural properties of PGA, PLA, and PLGA allows the polymers to be used for a wide variety of applications within the human body. These polymers are then used for drug-delivery systems, to construct synthetic scaffolding, etc. The amorphous form of PLA is used for drug delivery applications, while the crystalline form is good for building scaffolding and other biodegradable structures [62]. The

scaffolding is then implemented to allow growth of new tissues replacing damaged ones in the body. The scaffolding gradually erodes away as cells begin to grow and replace lost tissue around the region. Using a lower molecular weight polymer can speed up degradation.

The mechanical toughness and strength of the semi crystalline form of PLA and PGA is exploited for use in orthopedic devices.

The most common method of commercial production of PLA and PGA is by utilizing ring-opening polymerization combined with an insertion mechanism using a metal oxide [62].

2.5.5.3. Polydimethyl siloxane:

Polydimethyl siloxane (PDMS) is used in pacemakers and the delivery of vaccines. PDMS is an amorphous structure with low cross-linked elasticity. As a vulcanized rubber it cannot be melted or dissolved. The glass transition temperature of PDMS is very low (-123.15°C), and the polymer is very permeable to gases. The low glass transition temperature allows for fast molecular relaxation, which is beneficial for molding applications.

PDMS is used in numerous beneficial applications. For example, PDMS became an essential ingredient for use in glass eyes in World War II. Prior to the inception of localized drug delivery within the human body, antigens had to be taken orally and it was difficult, if not impossible to simulate local immune response in the body. This principle of localized drug delivery using PDMS comes into play in radical prostatectomy and radiation therapy for treatment of prostate carcinoma [64].

For the delivery of the vaccine, biodegradable pellets made of PDMS are used. The pellets are very small in diameter and generally contain soluble antigens to be released

within the body. The pellets consist of vulcanized rubber and have a mean diameter of 188 μm which allows for the particles to stay in the localized region. Drug release is controlled “ by the relative magnitude of the velocity of macromolecular relaxation to the velocity of drug diffusion through the rubbery region [64].

One method for the production of dimethyl siloxane starts with the monomer, dichlorodimethylsilane. Hydroxyl groups, through hydrolysis, replace the two chlorines in the monomer. To achieve a higher molecular weight, however, a different approach is used. This new method is done by a “ base catalyzed ring-opening polymerization of the siloxanes [62].

2.5.5.4. Polyethylene (PE) and Polymethylmethacrylate (PMMA):

Polyethylene, thermoplastic polymer, can be used as biomaterials. Depending on the structure and molecular organization of the polymer chains, thermoplastics may be semi-crystalline or highly crystalline.

Joint replacements, particularly at the hip and knee, and bone fixation devices have become very successful applications of materials in medicine. The use of pins, plates, and screws for bone fixation to aid recovery of bone fractures has become routine, with the number of annual procedures approaching five million in the USA alone [65].

Hip-joint replacements are principally used for structural support. Consequently, materials that possess high strength, such as metals, tough plastics, and reinforced polymer-matrix composites dominate them. In addition, biomaterials used for orthopedic applications must have high modulus, long-term dimensional stability, high fatigue resistance, and biocompatibility (i.e., there should be no adverse tissue response to the implanted device). Early developments in this field used readily available materials such as stainless steels, but evidence of corrosion after implantation led to their replacement by

more stable materials, particularly titanium alloys, cobalt-chromium-molybdenum alloys, and carbon fiber-reinforced polymer composites [64]. A typical modern artificial hip consists of highly polished cobalt-chromium ball connected to a titanium alloy stem that is inserted into the femur and cemented into place by in situ polymerization of polymethylmethacrylate (PMMA).

Consequently, much research on the development of hip-joint materials has been devoted to optimizing the properties of the articulating components in order to eliminate surface wear. Other modifications include porous coatings made by sintering the metal surface or coatings of wire mesh or hydroxyapatite; these promote bone growth and integration between the implant and the host, eliminating the need for acrylic bone cement [64].

2.5.5.5. Polytetrafluoroethylene:

PTFE is a thermosetting polymer which very limited application in medicine, but its characteristic properties, which combine high strength and chemical resistance, are useful for some orthopedic and dental devices. It also has high modulus and tensile properties with negligible elongation. The polymer chains in this material are highly cross-linked and therefore have severely hindered; this limits extension of the polymer chains under an applied load.

PTFE is used in many blood-contacting devices. These include artificial heart valves, synthetic vascular grafts, ventricular assist devices, drug releases, and a wide range of invasive treatment and diagnostic systems.

Artificial heart valves and vascular grafts, while not ideal, have been used successfully and have saved thousands of lives. However, the risk of thrombosis has limited the success of existing cardiovascular devices and has restricted potential application of the

PTFE to other devices [65]. Considerable advances have been made in the ability to manipulate molecular architecture at the surface of materials by using chemisorbed or physisorbed mono-layer films. Such progress in surface modification, combined with the development of nano-scale probes that permit examination at the molecular and sub-molecular level, provide a strong basis for optimism in the development of specialty biomaterials with improved blood compatibility [65].

2.5.5.6. Polyurethane:

2.5.5.6.1. Polyurethane properties as a biomaterial

PU is seen in everyday uses such as shoe soles, tires and foams, polyurethane holds an extremely import role in cardiac medicine today. Polyurethane is a thermoset non-condensation step growth polymer [62]. Polyurethane has a very low molecular weight compared to many other polymers with a molecular weight average of around 47,000 g/mol. The benefits of this material lie in the basics of it visible physical properties. Polyurethane is often described to bridge the gap between rubber and plastic. It holds one of the best load-bearing capacities of almost any materials around [64]

When compared to other plastics, polyurethanes are outstanding in strength, flexibility and fatigue resistance. They can be cast at only slightly elevated temperatures and are relatively biocompatible. Polyurethanes combine excellent mechanical properties with good blood compatibility, which has favored their use and development as biomaterials, particularly as components of implanted devices.

They also have the following properties:

- Wide range of flexibility combined with toughness.
- High abrasion resistance.
- High chemical resistance.
- High acid etch resistance.
- Excellent weatherability.
- Very low temperature cure.

2.5.5.6.2. Polyurethanes in Hip Replacement Prosthesis:

2.5.5.6.2.1. Introduction:

The hip joint is one of the largest weight-bearing joint of the body. Most of the human activities like walking, jumping, sitting etc. depend on the hip as it provides mobility along with stability. In everyday life the hip moves millions of times (to do the above activities) without even knowing, but once it gets damaged not only hip becomes stiff the walk with a painful limp and every step needs considerable effort [65].

Replacement of hip joint is a well established and a very successful operation for the last 40 years in which the diseased hip joint is replaced with an artificial one. It not only provides the freedom from pain and stiffness, but also improves quality of life. This specialized operation is now very successful and has been accepted very well both by the medical fraternity and the society. Figure 2.8 shows both the healthy and the arthritic hip joints.

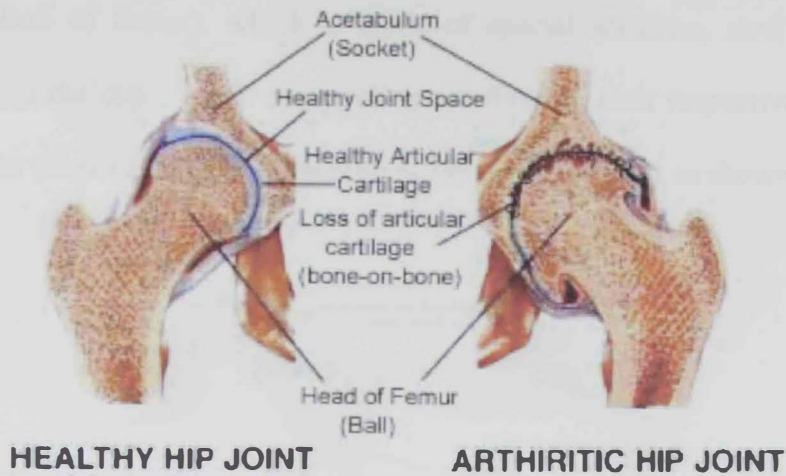


Figure 2.8: Healthy and arthritic hip joints.

2.5.5.6.2.2. What is a normal hip?

Normal hip joint consists of a round head (ball) of thighbone joining the acetabulum (socket / cup) at the pelvis in a ball-and-socket arrangement. A healthy joint is a remarkable mechanism due to the perfect matching of ball with the socket. A smooth and strong layer of articular cartilage (like velvet) aids it. This lining acts as a padding to absorb stresses and ensure almost frictionless movements of the hip joint. The hip joint is designed to withstand a lifetime of strenuous activity; However, arthritis of hip joint causes erosion of this velvet layer (cartilage layer), leading to pain, stiffness and difficulty in walking.

2.5.5.6.2.3. What is an artificial hip joint?

Like the normal hip joint the artificial hip joint also consist of two parts:

1. Sockets (or cup) which is made of special plastic usually ultrahigh molecular weight polyethylene (UHMPE) to give smooth surface to the head of femur.

2. Head (or Ball of femur), which is made of special stainless, steel alloy and fits perfectly into the cup. These components are fixed to their respective places during surgery after proper cutting and reaming of the damaged joint as shown in figure 2.9.

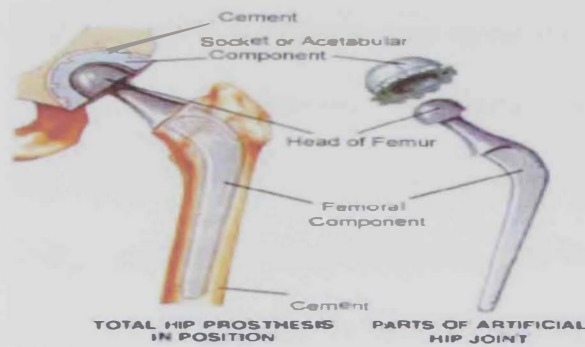


Figure 2.9: Parts of the artificial hip joint.

2.5.5.6.2.4. What are the types of Artificial Hip Joint?

The artificial hip joints are broadly divided on the basis of their fixation with the bone.

- i- *Cemented total hip* is the one where the components are fixed in pelvis and thighbone with bone cement.
- ii- *Uncemented total hip* prosthesis does not require bone cement for fixation, rather it is snugly fitted. This implant has the potential to allow bone to grow into it and therefore preferred in younger patient.
- iii- In some cases only femur may be fixed with cement and the socket is cementless. This prosthesis is known as *Hybrid total hip* [65].

2.5.5.6.2.5. Developments of the hip replacement prosthesis:

In joint replacement, typical patients are age 55 or older and suffer from debilitating rheumatoid arthritis, osteoarthritis, or osteoporosis. Orthopedic surgeries for artificial

joints exceed 1.5 million each year, with actual joint replacement accounting for about half of the procedures. A major focus of research is the development of new biomaterials for artificial joints intended for younger, more active patients.

Hip-joint replacements are principally used for structural support. Consequently, they are dominated by materials that possess high strength, such as metals, tough plastics, and reinforced polymer-matrix composites. In addition, biomaterials used for orthopedic applications must have high modulus, long-term dimensional stability, high fatigue resistance, long-term biostability, excellent abrasion resistance, and biocompatibility (i.e., there should be no adverse tissue response to the implanted device) [64]. The articulating component of the joint consists of an acetabular cup made of tough, creep-resistant, ultrahigh-molecular-weight polyethylene (UHMWPE). Abrasion at the ball-and-cup interface can lead to the production of wear particles, which in turn can lead to significant inflammatory reaction by the host. Consequently, much research on the development of hip-joint materials including this thesis has been devoted to optimizing the properties of the articulating components in order to eliminate surface wear [64]. Other modifications include porous coatings made by sintering the metal surface or coatings of wire mesh or hydroxyapatite; these promote bone growth and integration between the implant and the host, eliminating the need for acrylic bone cement [65].



Chapter Three

Materials and Sample Preparation



Materials and Sample Preparation:

3.1. Materials:

The reagents used in this study were 4,4'-diphenylmethane diisocyanate (MDI; Aldrich), polycaprolactone diols with molecular weights of 1250 (PCL1250) and 2000 (PCL2000; Aldrich), polypropylene glycols with molecular weights of 725 (PPG725) and 2000 (PPG2000; Aldrich), dipoly (ethylene glycol) adipate (DPEGA900; Aldrich), polyether glycol (PEG2000; Aldrich) with 1,4-butane diol (BD; Aldrich) chain extender. Tetrahydrofuran (THF) was used as received from Aldrich.

3.2. Synthesis of Polyurethanes:

The polymerization reaction was carried out under air according to the reaction scheme shown in figure 3.1.

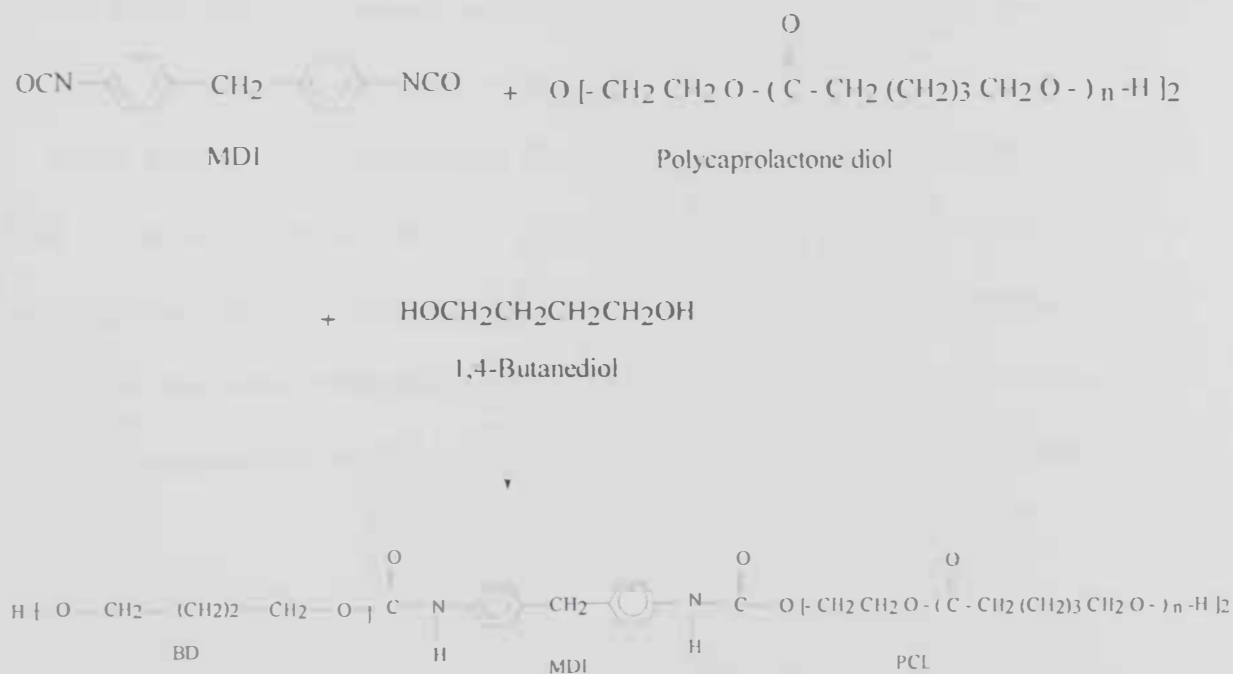


Figure 3.1: The schematic presentation for the preparation of polyurethane.

All polyurethane samples were synthesized in bulk polymerization. The diisocyanate and polyol were heated separately to 45-50°C until they melted, then the polyol was added gradually with stirring to the molten diisocyanate with gentle heating to form the prepolymer. After 10 – 15 minutes of heating, the 1,4-butanediol chain extender was added to the formed prepolymer and heated to 70°C for further 5-10 minutes; to ensure all reagents mixed and reacted. The mixture was then transferred to a mold and placed for one hour in a hot-press preheated to 120°C. After one hour, the formed polymer was allowed to cool to room temperature. The polymer product was removed from the mold as solid plaque was obtained. Strips were cut for thermal characterization and hardness measurements. Paper cups (175 mm x 175 mm with height of 3 mm and 6 mm) were used for the initial polymerization to record the exotherm.

The polyurethanes synthesized with different soft segment contents are listed in tables 3.1 – 3.4. The soft segment content varied from 57.69 % to 73.33 %.

Where MDICL is an abbreviation for the polyurethane produced by the reaction of MDI + polycaprolactone diol + 1,4-butanediol, while MDIPPG using MDI + polypropylene glycol + 1,4-butanediol, MDIPEG for MDI + polyether glycol + 1,4-butanediol and MDIDPEGA using MDI + dipoly(ethyl glycol)adipate + 1,4-butanediol.

% Soft segment content = $\left[\frac{\text{wt. polyol}}{\text{wt. MDI} + \text{wt. BD} + \text{wt. polyol}} \right] \times 100$.

Table 3.1. List of Formulations of MDICL series:

No.	MDI (g)	PCLdiol (g)	BD (g)	SS%*	Mould temp.	Comments
MDICL1	10	33	2	73.33	110°C (paper cup)	MDI + PCL(2000), then BD
MDICL2	12	30	3	66.67	120°C (paper cup)	MDI + PCL(2000), then BD
MDICL3	12	30	3	66.67	100°C (paper cup)	MDI + PCL(1250), then BD
MDICL4	8	32	5	71.11	130°C (paper cup)	MDI + PCL(2000), then BD
MDICL5	15	33	7	60	120°C (hot press)	MDI + PCL(2000), then BD
MDICL6	12	33	5	66	120°C (hot press)	MDI + PCL(2000), then BD
MDICL7	12	33	5	66	120°C (hot press)	MDI + PCL(1250), then BD
MDICL8	12	33	2	70.2	120°C (hot press)	MDI + PCL(2000), then BD

* SS % = (weight of the polyol / total weight of the polymer) x 100

Table 3.2: List of Formulations of MDIPPG series:

No.	MDI (g)	PPG (g)	BD (g)	SS%	Mould temp.	Comments
MDIPPG1	12	30	4	65.22	120°C (Paper cup)	MDI + PPG(2000), then BD
MDIPPG2	8	33	5	71.74	110°C (Paper cup)	MDI + PPG(2000), then BD
MDIPPG3	8	32	5	71.11	120°C (Paper cup)	PPG + BD(2000), then MDI

Table 3.3: List of Formulations of MDIDPEGA series:

No.	MDI (g)	DPEGA (g)	BD (g)	SS%	Mould temp.	Comments
MDIDPEGA1	15	30	7	57.69	120°C (Hot press)	MDI + DPEGA(900), then BD

Table 3.4: List of Formulations of MDIPEG series:

No.	MDI (g)	PEG (g)	BD (g)	SS%	Mould temp.	Comments
MDIPEG1	12	33	5	66	120°C (hot press)	MDI + PEG(2000), then BD
MDIPEG2	15	33	5	62.3	120°C (hot press)	MDI + PEG(2000), then BD
MDIPEG3	8	32	5	71.1	120°C (hot press)	MDI + PEG(2000), then BD

3.3. Material characterization:

3.3.1. Thermal Analysis:

3.3.1.1. Thermogravimetric analysis (TGA):

Thermogravimetric analysis (TGA) was performed under a nitrogen atmosphere and a heating rate of 10° C/min using TA instruments GA 2950 with a balance sensitivity of 0.1 microgram and accuracy better than 0.1 %.

3.3.1.2. Differential Scanning Calorimetry (DSC):

Differential Scanning Calorimetry (DSC) is a commonly used tool to determine molecular organization changes, such as phase separation, glass transition and melting. The phase separation between soft and hard segments is the main reason for the polyurethanes' good physical properties. On the other hand, both the mechanical and thermal properties of polyurethanes can be affected dramatically by phase mixing. Interaction between the soft and hard segments can increase the glass transition temperature (T_g) of the soft segment and decrease the T_g of the hard segments.

A Perkin-Elmer differential scanning calorimeter (Pyris DSC-7) calibrated with indium was used to evaluate heat transitions of polyurethane samples. The samples (MDICL1, MDICL4, MDICL6 and MDICL7) were dissolved in hot tetrahydrofuran (THF), the polymers then precipitated by adding methanol drop wise to an excess of cold

methanol with continuous stirring. The solution was filtrated to get a white powder of the polymer, then dried in vacuum oven at 45°C. Circular samples with an average weight of 9- 15 mg were used for the measurements. The samples were scanned at a heating rate of 10°C/min under dry, oxygen-free, nitrogen flowing at flow rate of 50-60 ml/min. The samples were scanned from 50°C to 250°C.

3.3.2. Nuclear Magnetic Resonance (NMR) Analysis:

¹H NMR spectra of the polyurethanes in deuterated chloroform were recorded at 27°C with a Jeol model JNM-LA 300 FT-NMR and JNM-300MHz NMR spectrometer. Tetramethylsilane (TMS) was used as a reference and assigned a value of 0.00 ppm

3.3.3. Fourier Transform InfraRed (FT-IR) Spectroscopy:

IR spectra of the polyurethanes were recorded in transmission mode with a Nicolet FT-IR Magna-IR 560 system. The asymmetric stretching vibration of the NCO group at 2270 cm⁻¹ was used to determine the completeness of the cure.

3.3.4. Hardness test:

3.3.4.1. Definition:

It is the resistance of metal to plastic deformation, usually by indentation. However, the term may also refer to stiffness or temper, or to resistance to scratching, abrasion, or cutting. It is the property of a metal, which gives it the ability to resist being permanently, deformed (bent, broken, or have its shape changed), when a load is applied. The greater the hardness of the metal, the greater resistance it has to deformation. As well as, it can be defined as the resistance of material to indentation [66,67].

3.3.4.2. Hardness measurement methods:

There are many methods for measuring the hardness, but the common methods are:

1. Rockwell hardness test
2. Brinell hardness
3. Vickers
4. Knoop hardness
5. Shore

We use shore A for the determination of the samples hardness in this study.

3.3.4.3. Shore Hardness:

Shore hardness [66] is a measure of the resistance of material to indentation by 3 spring-load indenter. The higher the number, the greater the resistance.

The hardness testing of plastics is most commonly measured by the Shore (Durometer) test. Shore Hardness, using either the Shore A or Shore D scale, is the preferred method for rubbers/elastomers and is also commonly used for 'softer' plastics such as polyolefins, fluoropolymers, and vinyls. The Shore A scale is used for 'softer' rubbers while the Shore D scale is used for 'harder' ones. The shore A can be determined with an instrument called a Shore A Durometer. If the indenter completely penetrates the sample, a reading of zero is obtained, while if there is no penetration occurs, a reading of 100 will be displayed. The reading is dimensionless.

The hardness value is determined by the penetration of the Durometer indenter foot into the sample. The results obtained from this test are a useful measure of relative resistance to indentation of various grades of polymers. However, the Shore Durometer hardness test does not serve well as a predictor of other properties such as strength or

resistance to scratches, abrasion, or wear, and should not be used alone for product design specifications [68].

For the polyurethanes to be biocompatible material for specific medical application, they must possess some properties such as the hardness which should be in the range of 70 – 80 shore A [66].

The hardness of most polyurethane samples were measured using Type D Durometer, Conforms to ASTM 2240 – 75 model 307 L. Figure 3.2 shows the range of the hardness of thermoplastic polyurethanes TPU (Elastollan) in comparison to other materials using shore test.

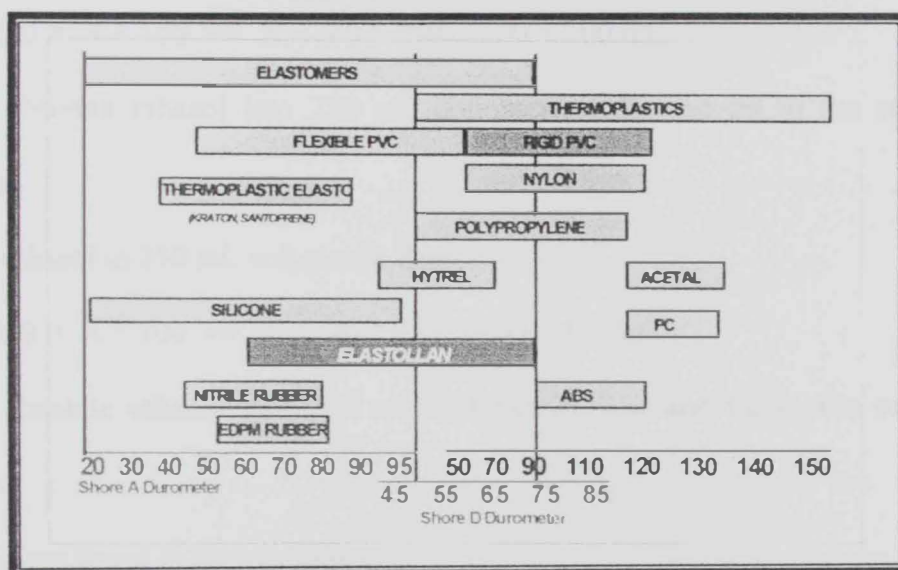


Figure 3.2: Hardness comparison of TPU (Elastollan) and other materials.

3.3.5. Histology experiments:

The samples LPUPC, MDICL4 and MDICL8 were implanted under the skin of three individual rats and one rat was used as a control for comparison purposes. The three samples were kept in the rats for 48 hours, then the polymer samples were taken out from underneath the skin and put in formalin solution that was prepared according to the ratio

given below. The polymers were washed with water six times for six hours and kept in 70 % ethanol overnight. The following day the polymers were dehydrated using a series of alcoholic solutions containing:

100 % ethanol, 90 % ethanol, 80 % ethanol, 70 % ethanol and 96 % ethanol that had been prepared from the absolute ethanol as follow:

For 90 % ethanol in 250 mL volumetric flask:

$$90 * 250 = X * 100 \Rightarrow X = (90 * 250) / 100 = 225 \text{ mL}$$

225 mL of absolute ethanol into 250 mL volumetric flask and fill to the mark with distilled water.

For 80 % ethanol in 250 mL volumetric flask:

$$80 * 250 = X * 100 \Rightarrow X = (80 * 250) / 100 = 200 \text{ mL}$$

200 mL of absolute ethanol into 250 mL volumetric flask and fill to the mark with distilled water.

For 70 % ethanol in 250 mL volumetric flask:

$$70 * 250 = X * 100 \Rightarrow X = (70 * 250) / 100 = 175 \text{ mL}$$

175 mL of absolute ethanol into 250 mL volumetric flask and fill to the mark with distilled water.

96 % ethanol was found in the laboratory.

The polymers were washed starting with 70 % ethanol, 80 % ethanol, 90% ethanol once each, then 96 % ethanol, twice followed by 100 % ethanol, twice.

The three treated polymer samples and the original sample of LPUPC , MDICL4 and MDICL8 were kept in absolute ethanol for surface examination using scanning electron microscopy.

While the tissues were cut and immersed in 10 % formalin solution that had been prepared as follow:

0.4 g of sodium dihydrogen phosphate (NaH_2PO_4) and 0.65 g of disodium hydrogen phosphate (Na_2HPO_4) were dissolved in 15 ml distilled water. 10 mL of formaldehyde were added to the solution which was made up to 100 mL using distilled water in a volumetric flask. The tissues, then, were processed as follow: (14 to 16 hours).

They were transferred into the following solutions:

- Buffer
- 50 % alcohol (ethanol), one hour.
- 70 % alcohol, two hours.
- 95 % alcohol, three changes, two hours each.
- Absolute alcohol (100 %), 3 changes, two hours each.
- Xylene, three changes, two hours each.
- Paraffin, four changes, two hours for the first two changes and then one hour for the third and the fourth changes.
- Paraffin, under vacuum, two hours [69].

After processing, the tissues were placed in blocks of wax for cutting thin sections of those samples. Putting the blocks in the softener (comfort solution) for one hour to soften them. Using a microtome with a sharp knife to make the sections from those blocks, then each section was placed in 50 % alcohol followed by distilled water in 47°C to make the sections straight. Each section was placed on a slide for staining and eventual scanning.

All slides were placed in an oven at 60°C for 20 – 25 minutes in order to remove any traces of alcohol and water. Staining procedure was performed by placing the samples in:

- Xylene 1 and Xylene 2, two minutes each for dewaxing.
- Absolute ethanol (100 %), 95 % ethanol and 70 % ethanol, one minute each for rehydration.

- Distilled water, one minute.
- Hematoxyline, four minutes.
- Tap water, few dips.
- Acidified ethanol (300 ml of ethanol + 3 ml of HCl), few dips for decoloring.
- Tap water, five – ten minutes.
- Eosin, thirty seconds.
- 70 % ethanol and 95 % ethanol, fifteen seconds each.
- 100 % ethanol, two changes, one minute each for dehydration.
- Xylene 2 and Xylene 1, two minutes each for clearing [69].

The slides were subjected to a mounting procedure which involved adding a mounting medium to the slides, covering with cover slips and placing the slides in an air chamber to dry.



3.3.6. Scanning Electron Microscopy (SEM):

SEM was conducted on a Jeol model JSM-5600 instrument at an accelerating voltage of 10KV and 18-300 000 magnification with guaranteed resolution of 3.5 nm. Samples were dehydrated using ethanol, dried on air and then sputter-coated with a thin film of gold.



Chapter Four

Results and Discussion



4.1. Thermal properties:

4.1.1. Thermogravimetric analysis (TGA):

Since mechanical properties are largely influenced by morphology, the thermal properties of the polymers were investigated. Thermogravimetric analysis (TGA) has been used to examine the thermal stability of the polymers obtained. The thermal stability was examined over a temperature range between 25-700°C at heating rate of 10°C/min and flow rate of 50 cm³/min of nitrogen gas. The 5% weight loss in air is at around 310°C, almost identical for samples MDICL1 and MDICL4, and at around 280°C for samples MDICL6 and MDICL7. This indicates that the thermal stability of the LPU based segmented polyurethanes with the same soft segment concentration depend on thermal stability of the urethane bond, which is the weakest linkage in the polyurethane structure. The degradation in air is a three-step process, illustrated in figure 4.1 which is the thermal weight loss curve for sample MDICL1. It was observed that the first weight loss occurs at temperature range of 280 – 350°C with 55.7 % weight loss which was the maximum weight loss followed by 39 % weight loss at temperature range of 360 – 430°C. The minimum weight loss (5.3 %) occurs at 440 – 500°C.

For all samples the thermal degradation pattern was almost identical. Figure 4.2 shows the TGA thermogram of MDICL4 which starts to degrade at a temperature range 280 – 430°C with 89 % weight loss (the maximum weight loss). The next weight loss (6%) occurs at 440 – 460°C and in the temperature range of 470 – 610°C, the weight loss was 5 % (the minimum weight loss).

Similar thermal degradations were observed for MDICL6 and MDICL7 samples (figures 4.3, 4.4) with varying weight loss and temperature ranges. First 88 % weight loss occurs at 280 – 420°C for MDICL6 and 90 % weight loss at 280 – 425°C for MDICL7.

The second weight loss occurs at 430 – 475°C for both samples (5 % and 7.5 % for MDICL6 and MDICL7 respectively). The last weight loss of 7 % and 2.5% occurs at a temperature range of 480 – 620°C.

Figure 4.5 shows the TGA thermograms of all polyurethane samples. It was observed that the onset of thermal decomposition of the polymer backbone occurs at 280°C. Before 280°C, there is no appreciable weight loss, which indicates that these polymers were very stable over a wide temperature range and are suitable for medical or other applications within this range. Above 350°C, a rapid weight loss is possible and complete decomposition was observed beyond 500°C.

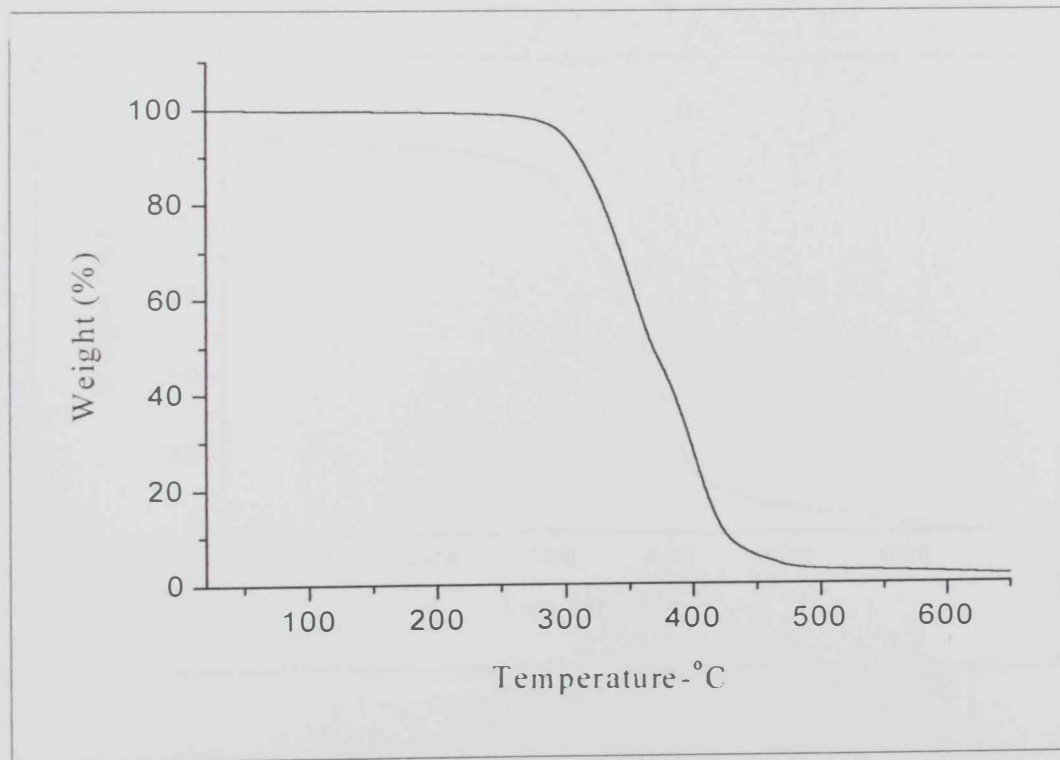


Figure 4.1: TGA thermogram of MDICL1.

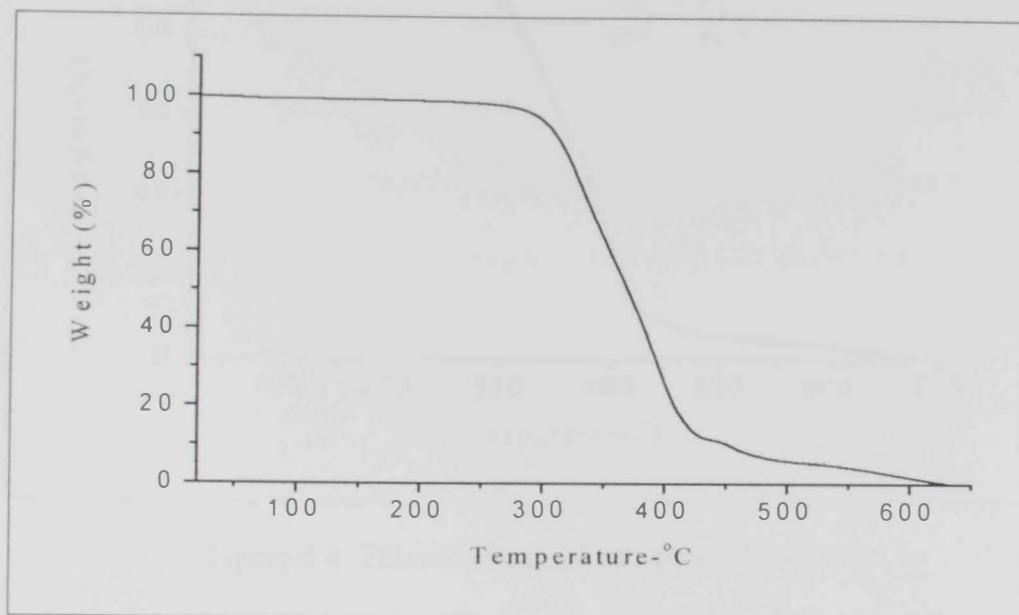


Figure 4.2: TGA thermogram of MDICL4.

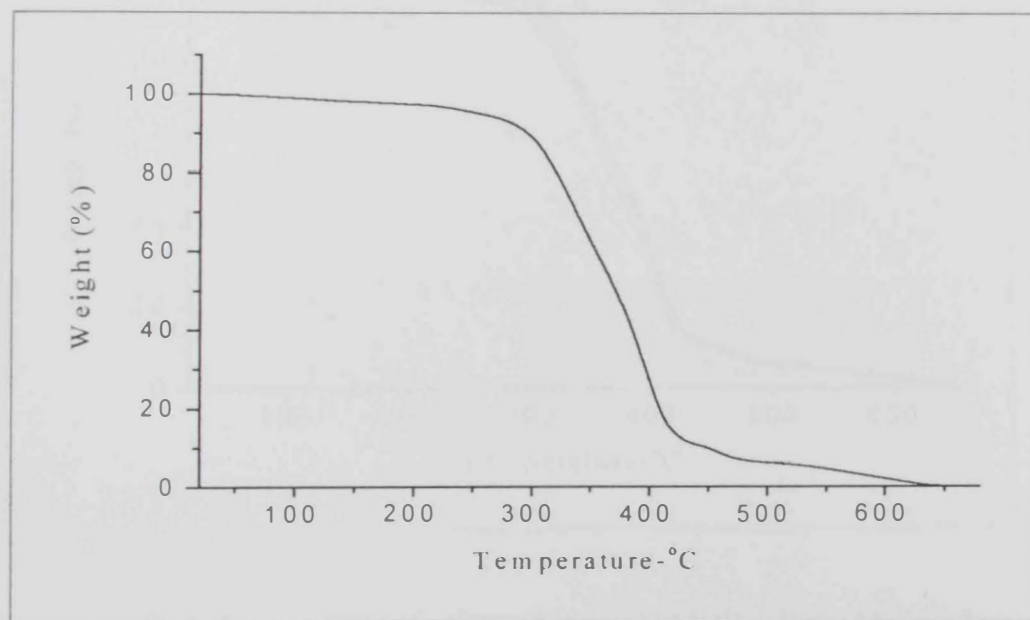


Figure 4.3: TGA thermogram of MDICL6.

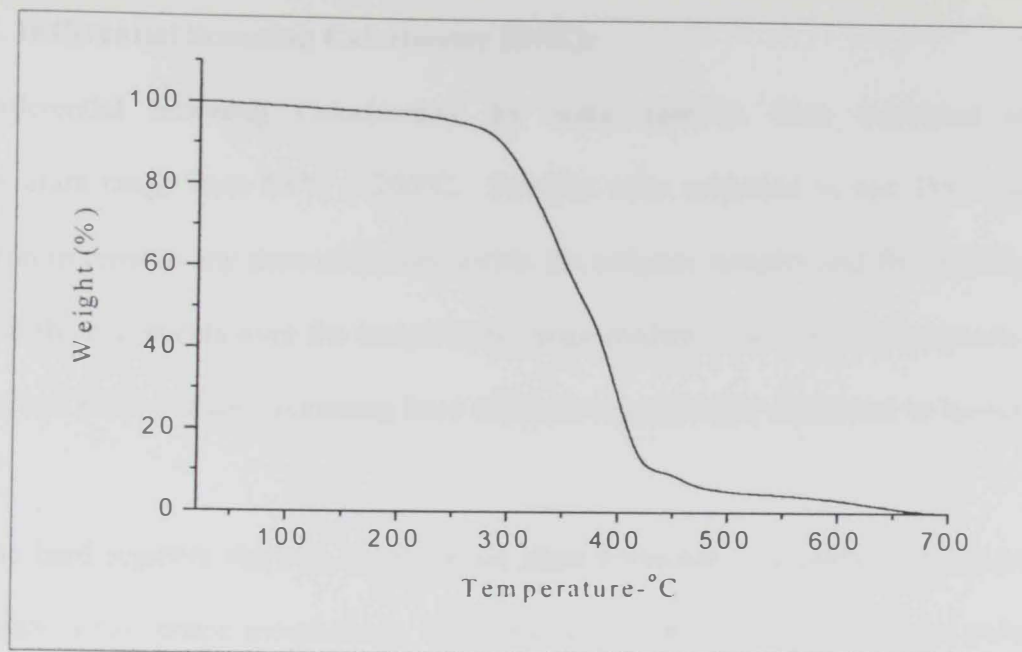


Figure 4.4: TGA thermogram of MDICL7.

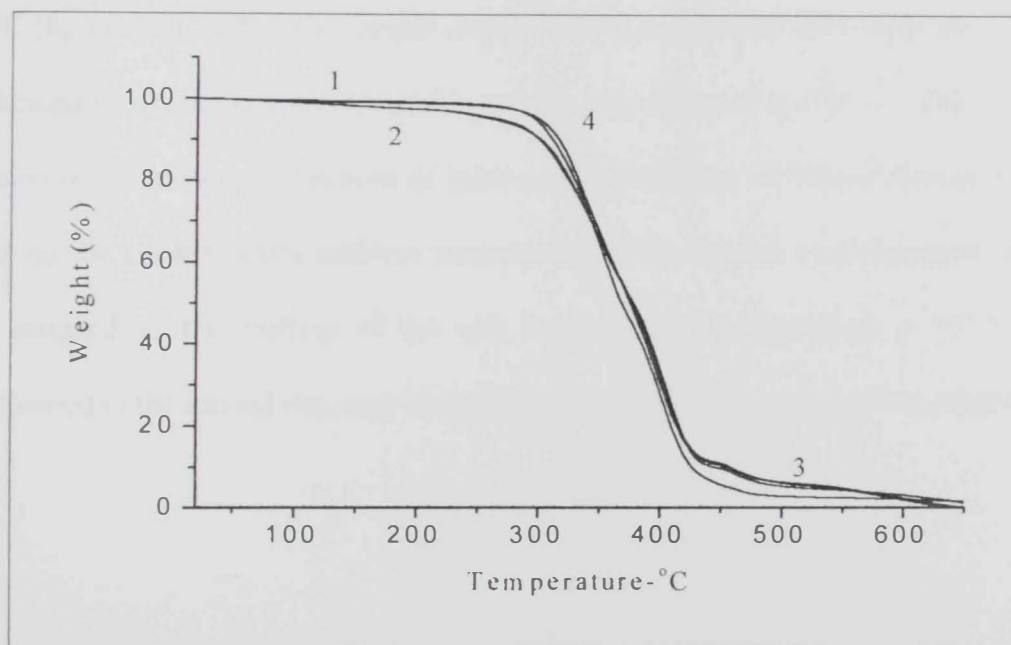


Figure 4.5: TGA thermograms of polyurethanes: (1) MDICL1; (2) MDICL4; (3) MDICL6 and (4) MDICL7,

4.1.2. Differential Scanning Calorimetry (DSC):

Differential Scanning Calorimetry for some samples were evaluated over a temperature range from 55°C – 200°C. Samples were subjected to two DSC runs, the first run to remove any thermal history within the polymer samples and the second run to see the thermal events over the temperature range studied. The DSC thermograms of the segmented polyurethane containing hard and soft segments are illustrated in figures 4.6 – 4.8.

The hard segment showed a very broad glass transition, suggesting that the polymer possesses a two-phase morphology. Since the T_g of the soft segment in the polymer is below the room temperature, the phase separation between the soft and the hard is not complete.

MDICL4 sample exhibited two clearly identified endothermic events at 133°C and at 172°C (figure 4.6). When the sample reaches 200°C and cooled afterwards down to 55°C and heated up again, only one thermal transition was observed at 172°C. The T_g was not detected on these samples because of instrumental limitation with liquid nitrogen where it could not be cooled below ambient temperature. The thermal transition peak at 172°C was assigned to the melting of the soft segments. The transition at 133°C, which disappeared in the second run, may be attributed to insufficient curing of the sample.

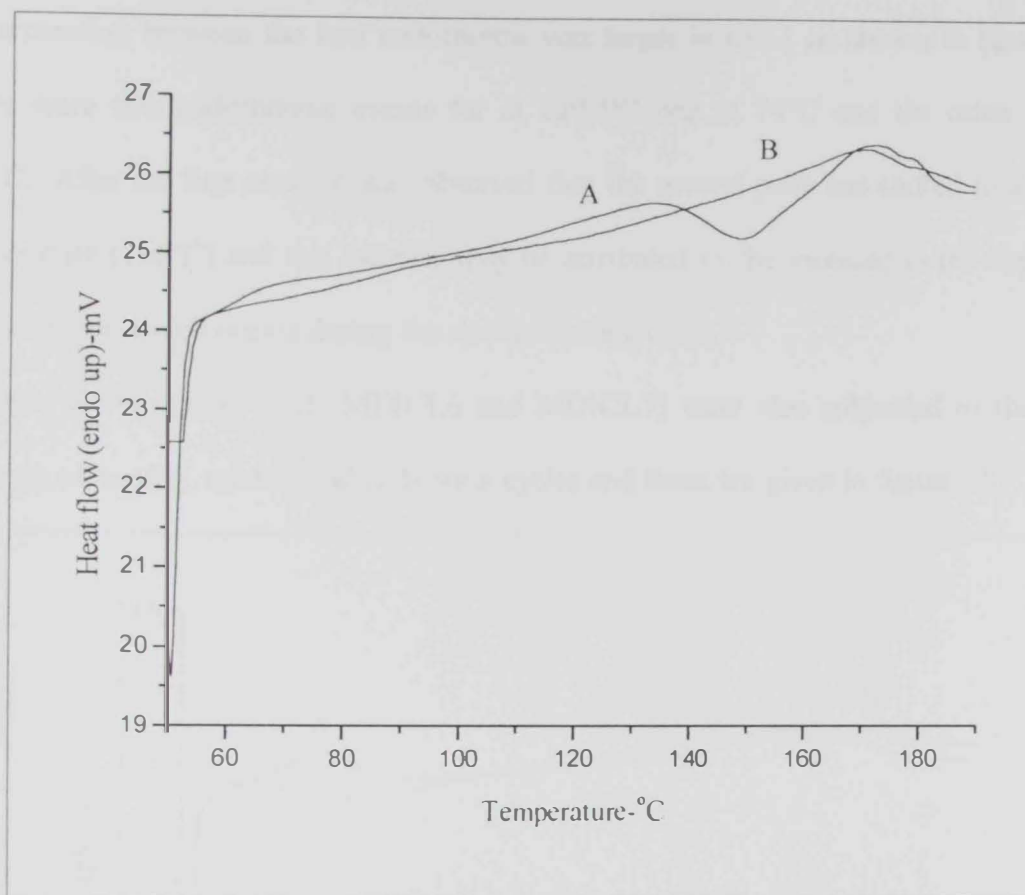


Figure 4.6: DSC thermograms for sample MDICL4 (A) run 1-
heating and (B) run 2-reheating

Similar thermal behavior was observed for the standard sample (LPUPC) except that the separation between the two endotherms was larger in run 1 as shown in figure 4.7. There were two endothermic events for at LPUPC one at 74°C and the other one at 156°C. After the first rerun, it was observed that the second peak has shifted to a higher temperature (166°C) and this increase may be attributed to the increase in the degree of crystallization which occurs during the slower cooling cycle.

Other samples (MDICL1, MDICL6 and MDICL7) were also subjected to the same program of heating, cooling and re-heating cycles and these are given in figure 4.8.

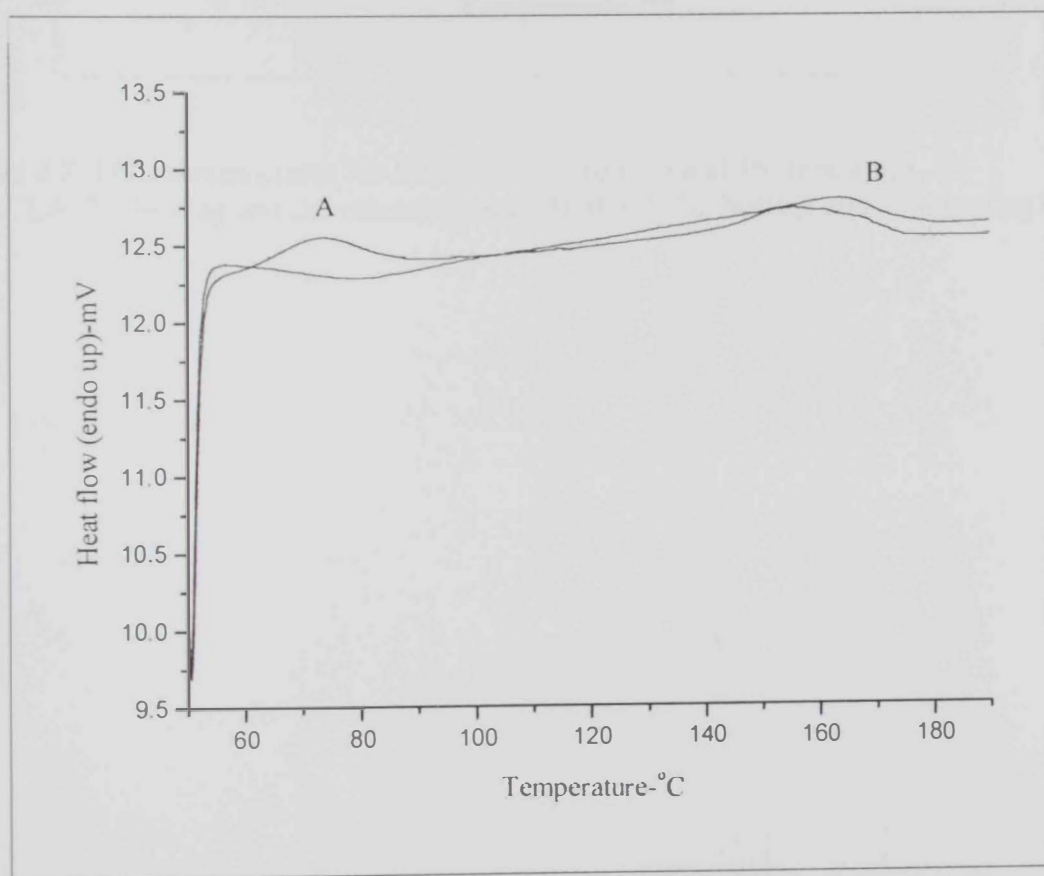


Figure 4.7: DSC thermograms for sample LPUPC (A) run 1-heating and
(B) run 2-reheating

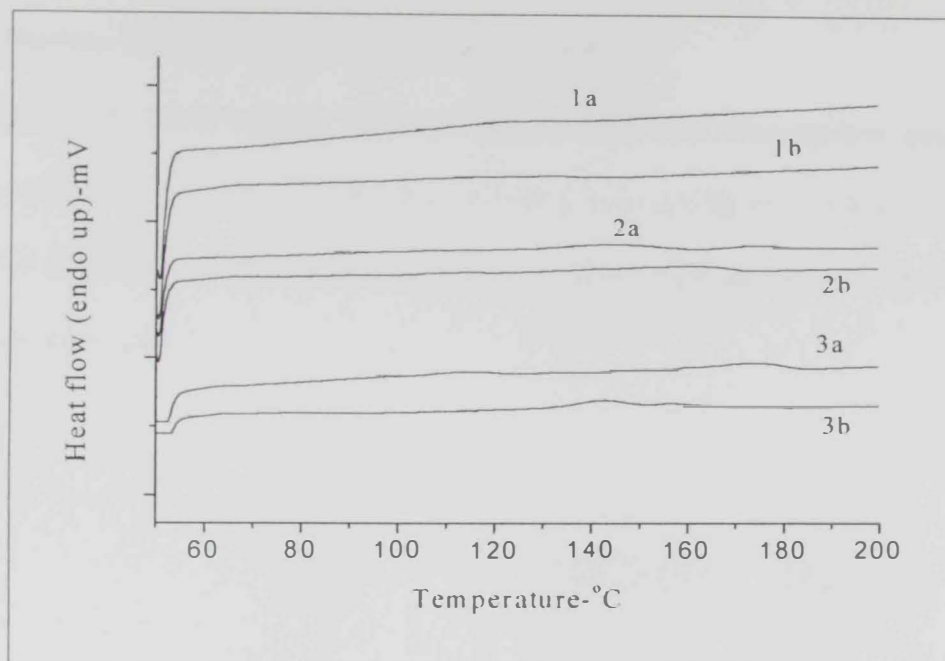


Figure 4.8: DSC thermograms for MDICL1 (1a: heating and 1b: reheating), MDICL6 (2a: heating and 2b: reheating) and MDICL7 (3a: heating and 3b: reheating)

4.2. Nuclear Magnetic Resonance (NMR) Analysis:

Typical ¹H NMR spectra of polyurethanes show five characteristic peaks at 1.2-1.6 ppm due to (-CH₂-), 2.25-2.30 (-CH₂-CO-O-), 3.61 (-CH₂-O-), 3.9-4.2 (-CH₂-O-CO-), and 7.0 (-NH-CO-) ppm. The aromatic protons from MDI showed at 7.18-7.2 ppm. as shown in figure 4.9.

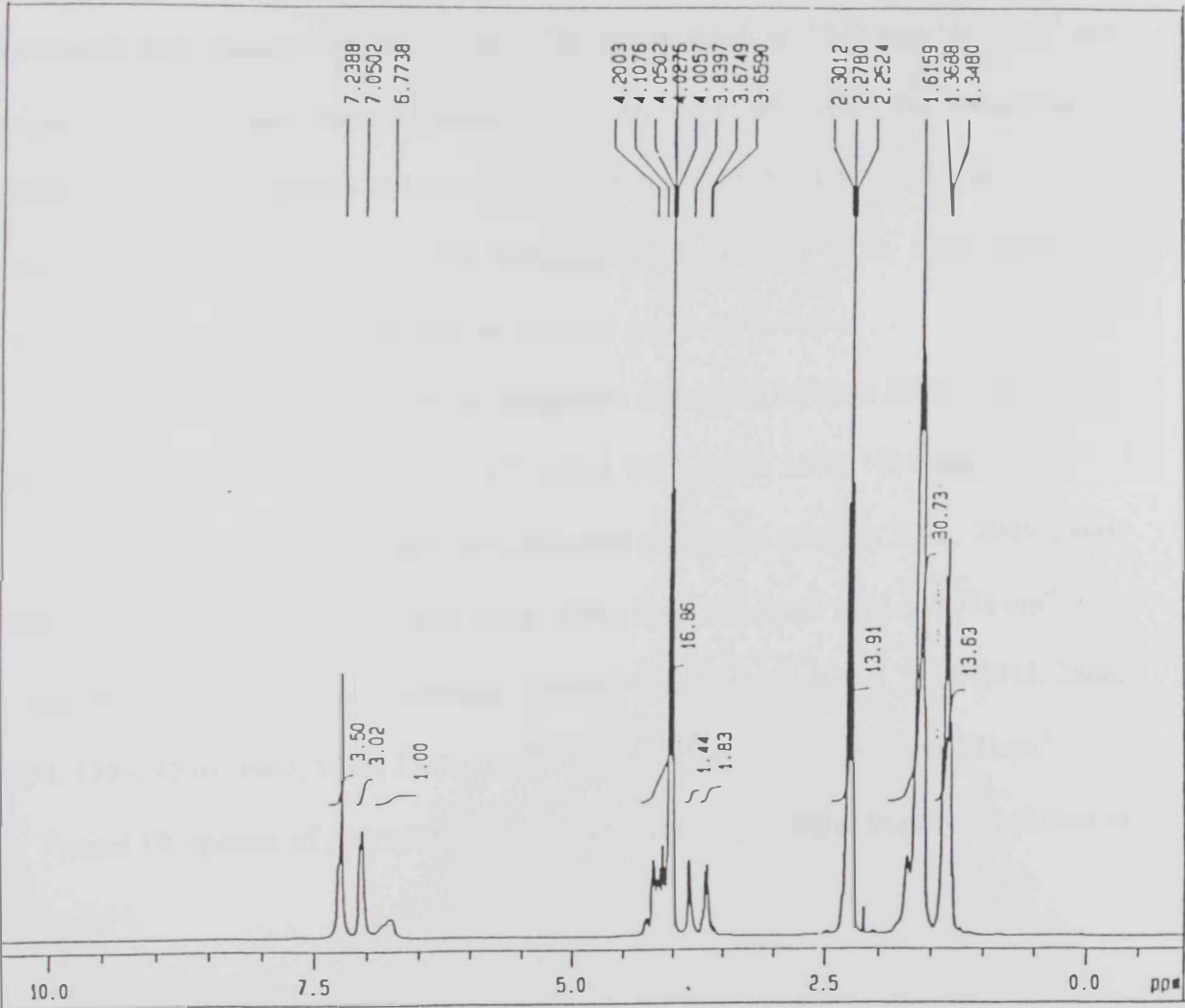


Figure 4.9: ¹H NMR spectrum of a polyurethane based on MDI, PCL2000 and BD.

4.3. Fourier Transform InfraRed (FT-IR) Spectroscopy:

Typical IR spectra of MDICL1 sample is shown in figure 4.10, there are distinctive absorption bands at 3378, 3342, 2946, 2865, 1732, 1597, 1533, 1461, 1414, 1392, 1357, 1310, 1222, 1165, 1066 and 1018 cm^{-1} . The absorption at 3342 cm^{-1} corresponding to hydrogen-bonded $-\text{NH}$ groups and a small shoulder at 3378 cm^{-1} can be attributed to nonbonded $-\text{NH}$ groups. The absorption band at 2946 and 2865 cm^{-1} are associated with asymmetric and symmetric $-\text{CH}_2$ groups. The strong bands at 1732 and 1597 cm^{-1} are assigned to the free and hydrogen-bonded $-\text{C}=\text{O}$ groups respectively. The absorption of $\delta(\text{NH})$ with $\nu(\text{CO-N})$ appears at 1533 cm^{-1} . The bands at 1461, 1414, 1392, and 1357 cm^{-1} manifest the various modes of $-\text{CH}_2$ vibrations. The bands at 1222, 1165, 1066 cm^{-1} are assigned to the stretching vibration of the ester group $-\text{CO-O-C-}$.

For MDICL4 (figure 4.11), there are distinctive absorption bands at 3333, 2946, 2866, 1731, 1597, 1536, 1461, 1414, 1391, 1357, 1310, 1228, 1165, 1079, 1018 and 772 cm^{-1} .

For MDICL6 (figure 4.12), there are distinctive absorption bands at 3322, 2945, 2866, 1731, 1597, 1536, 1460, 1414, 1392, 1358, 1311, 1225, 1066 and 1019 and 771 cm^{-1} .

For MDICL7 (figure 4.13), there are distinctive absorption bands at 3333, 2945, 2866, 1731, 1597, 1536, 1463, 1414, 1394, 1365, 1310, 1236, 1067 and 1018 and 771 cm^{-1} .

Typical IR spectra of polyurethanes with different polyol chain lengths are shown in figure 4.14.

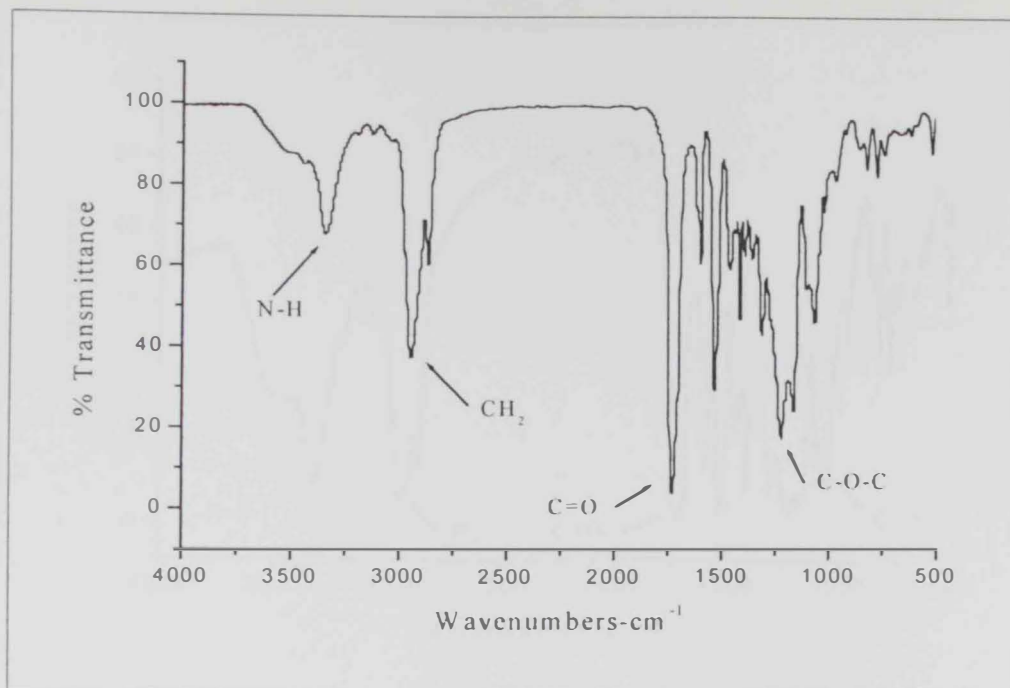


Figure 4.10: FTIR spectra for MDICL1.

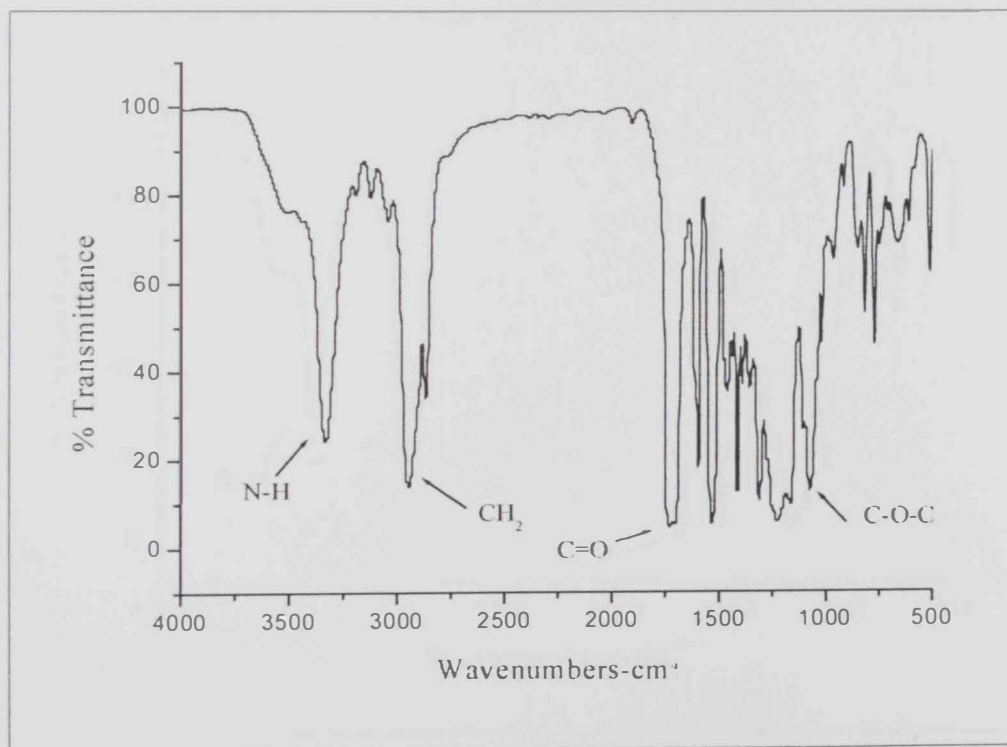


Figure 4.11: FTIR spectra for MDICL4.

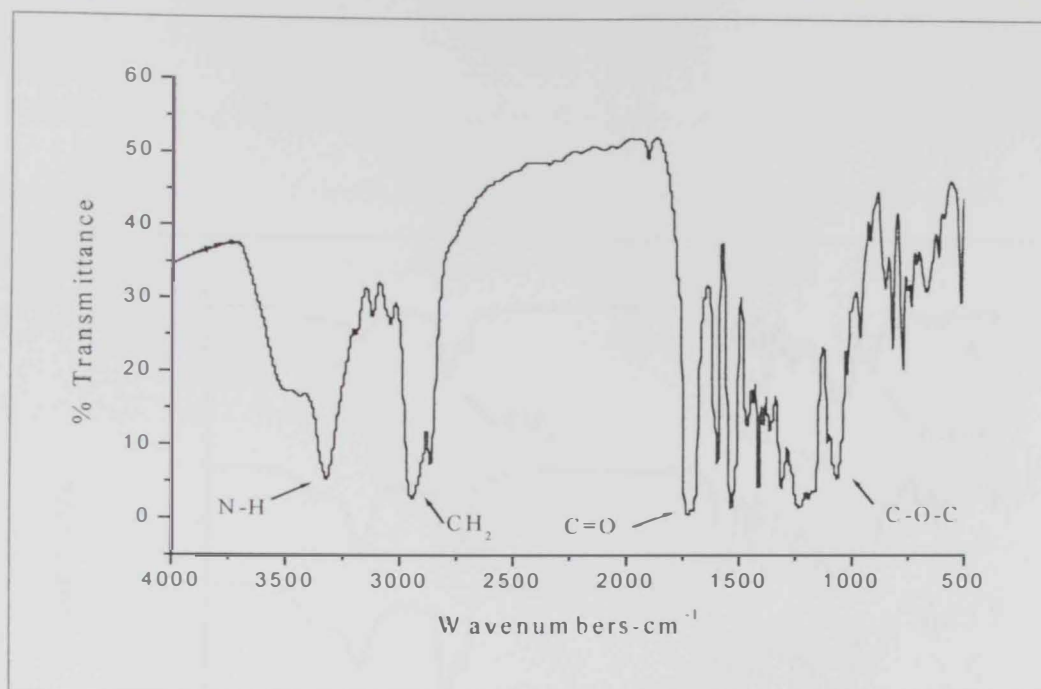


Figure 4.12: FTIR spectra for MDICL6.

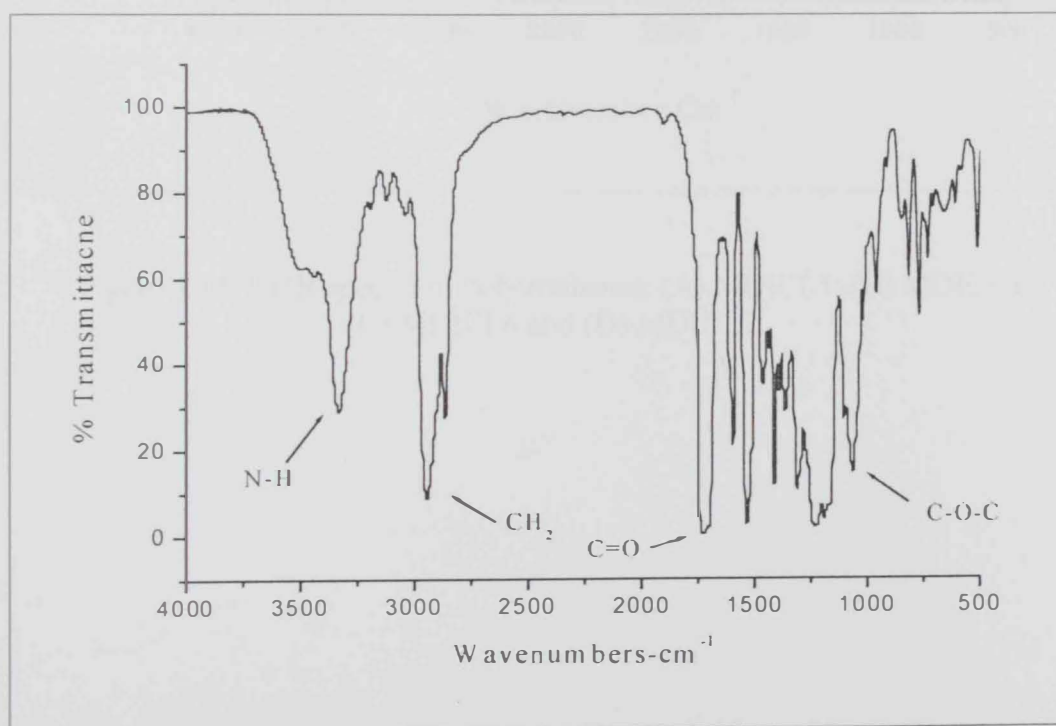


Figure 4.13: FTIR spectra for MDICL7.

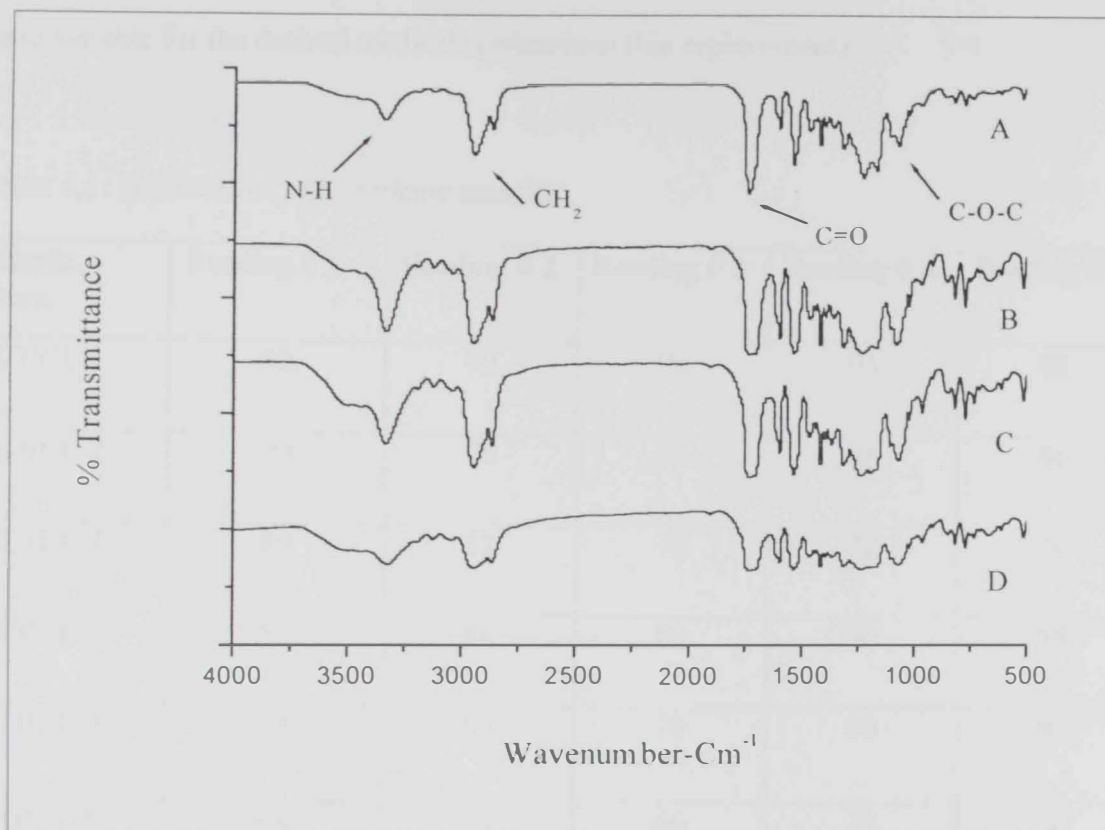


Figure 4.14: FTIR spectra of polyurethanes: (A) MDICL1; (B) MDICL4; (C) MDICL6 and (D) MDICL7.

4.4. Hardness Measurement:

Table 4.1 shows the hardness of most of the polyurethane samples synthesized in this study. It is clear that the hardness of polyurethane samples is in the range which make them suitable for the desired medical applications (hip replacement).

Table 4.1: Hardness of polyurethane samples

Sample Name	Reading # 1	Reading # 2	Reading # 3	Reading # 4	Reading # 5	Average
MDICL 1	92	90	96	94	98	94
MDICL 2	90	78	84	88	86	85.2
MDICL 3	80	82	78	72	70	76.4
MDICL 4	82	84	80	86	88	84
MDICL 5	63	65	70	66	69	66.6
MDICL 6	68	64	66	72	70	68
MDICL 7	66	70	62	58	64	64
MDICL 8	62	60	58	56	64	60
MDIPG 1	44	42	50	46	44	45.2
MDIPEGA 1	42	40	34	38	36	38
MDIPEG 1	64	62	52	56	58	58.4

4.5. Tissue reactivity in biological system:

4.5.1. Normal skin:

Histological examination of normal rat skin of rats shows three main layers (figure 4.15), which are the epidermis, the dermis and the hypodermis. The epidermis E consists of a stratified squamous keratinising epithelium which has a thick keratinised surface layer. The germinal layer of the epidermis is located at the basement membrane and adjacent to the dermal layer (figure 4.15). The keratinised layer consists of flattened fused cell remnants composed mainly of the fibrous protein, keratin (figure 4.15). The epidermis is supported by the dermis D, a layer of dense fibro-elastic tissue. The dermis merges with the loose supporting tissue of the hypodermis H which contains myotoms that are separated by collagenous myosepta. The junction between the epidermis and dermis is characterized by downward folds of the epidermis called epidermal or rate ridges which interdigitate with upward projections of the dermis called dermal papillae [70].

Two layers with rather indistinct boundaries have been described in the dermis. They are the outermost papillary layer and the deeper reticular layer. The papillary layer is thin and is composed of loose connective tissue. Besides fibroblasts, many connective tissue cells are present, the most abundant being the mast cells. Extravasated leukocytes and macrophages are also seen. The papillary layer is so called because it penetrates in the papillae. From this layer, collagenous fibrils insert into the basal lamina and extend perpendicularly into the dermis. They are thought to have a special function, binding the dermis to the epidermis, and are thus called anchoring fibrils. A layer of thin elastic fibers runs parallel to the basal cell layer of epidermis. The reticular layer is thicker, composed of irregular dense connective tissue, and therefore has more fibers and fewer cells than the papillary layer [71].

In the dermal layer hair follicles are impeded in fibro-elastic tissue. Micrograph (figure 4.16) illustrates the presence of fibrocytes in the connective tissue of the hypodermal layer. Mast cells as well as other white blood cells are also present (figure 4.16).

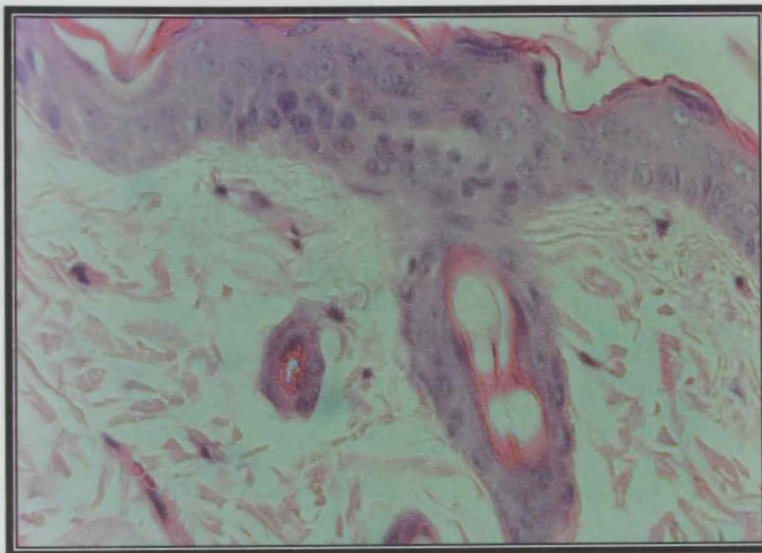


Figure 4.15: The epidermal and dermal layers of the control

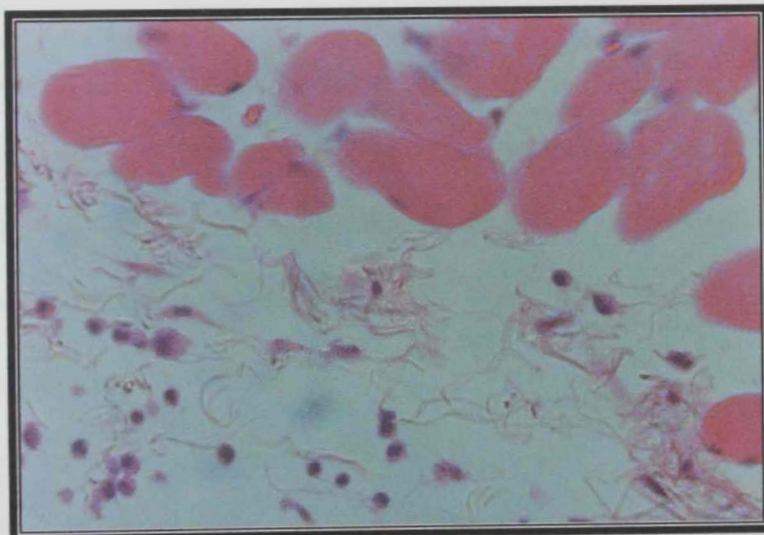


Figure 4.16: The hypodermal layer of the control.

4.5.2. Implantation of LPUPC sample:

Figure 4.17 shows mild lymphocytes infiltration as well as fibrocytes, mast cells and all types of white blood cells. So the subcutaneous implantation of LPUPC sample for 48 hours did cause some mild tissue reactivity as compared with the control sample (figure 4.16).

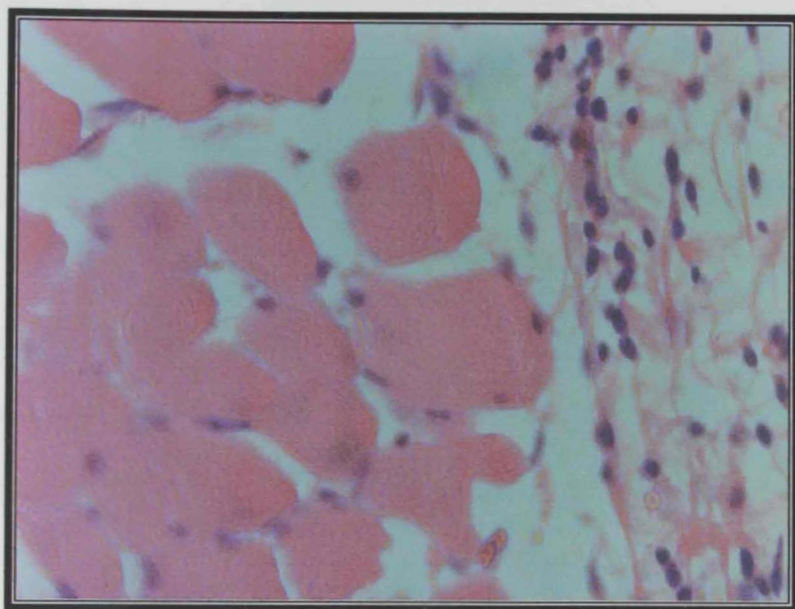


Figure 4.17: The implantation of LPUPC.

4.5.3. Implantation of MDICL8 sample:

Implantation of MDICL8 sample caused sever irritation and high lymphocyte infiltration in the hypodermis layer as indicated in figure 4.18. It is evident that a large number of invasive lymphocytes as well as blood cells leakage are present as compared with the control sample (figure 4.16).

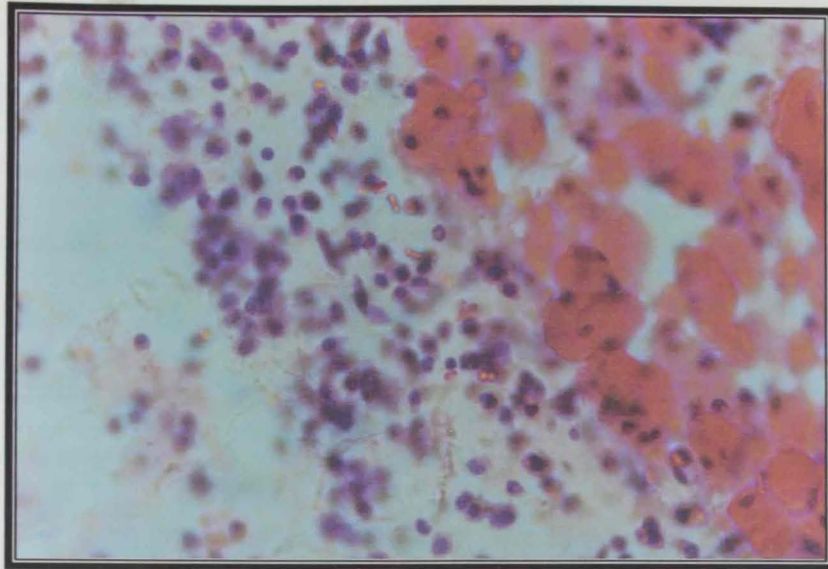


Figure 4.18: Implantation of MDICL8.

4.5.4. Implantation of MDICL4 sample:

Figure 4.19 shows normal fibrocytes and mast cells in the hypodermis layer when MDICL4 sample was implanted. MDICL4 implantation did not affect the epidermis and the dermis.

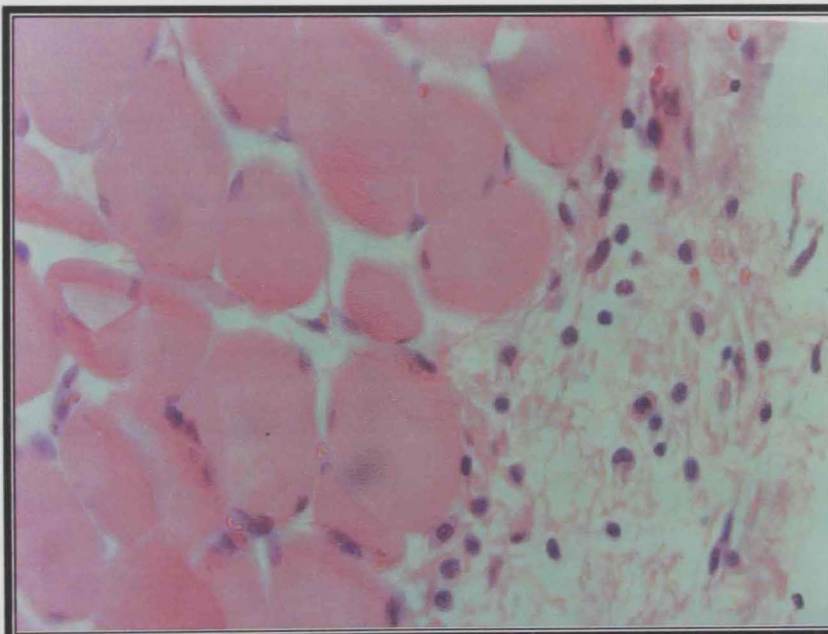


Figure 4.19: Implantation of MDICL4.

4.6. SEM:

Scanning electron micrographs of polyurethane polymers revealed a smooth surface without any appreciable crystal grains or pores (figure 4.20a). Higher magnification showed as expected, the surface of the polyurethane, which was composed of crystal and amorphous domains with two-dimensional arrangements.

Implantation of LPUPC polymer for 48 hours potentiate collagen fiber formation (figure 4.20b). It is clear that collagenous fibers covered the polymer surface with no cellular presence. MDICL4 polymer showed also fiber formation after 48 hours of implantation (figure 4.21b). Fiber accumulation on MDICL4 polymer surface was much more than LPUPC polymer. This may be attributed to the fact that the purity of MDICL4 polymer was lower than that of LPUPC polymer. In addition, MDICL4 polymer was partially cured as compared to LPUPC polymer.

In the present study, MDICL8 was used to show positive tissue reactivity. Indeed MDICL8 showed sever collagen fiber formation as compared to LPUPC and MDICL4 polymers (figure 4.22b). It is also evident that cells from connective tissue were found attached to this polymer surface. These data clearly indicate that both LPUPC and MDICL4 polymers were synthesized with similar methods and caused similar tissue reactivity; however, purity and curing were not similar.

Polyurethanes have been widely used for implantable medical devices, however; cyclogical and physical interactions of implanted polyurethane depend on morphology, which depends on thermal history during processing and devices manufacturing.

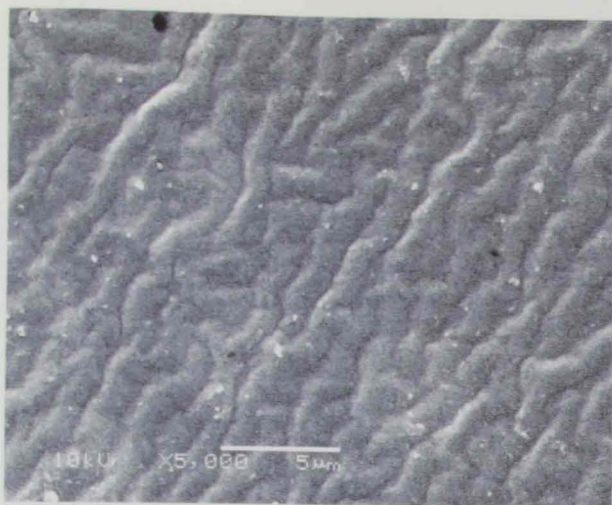


Figure 4.20a: SEM for normal LPUPC

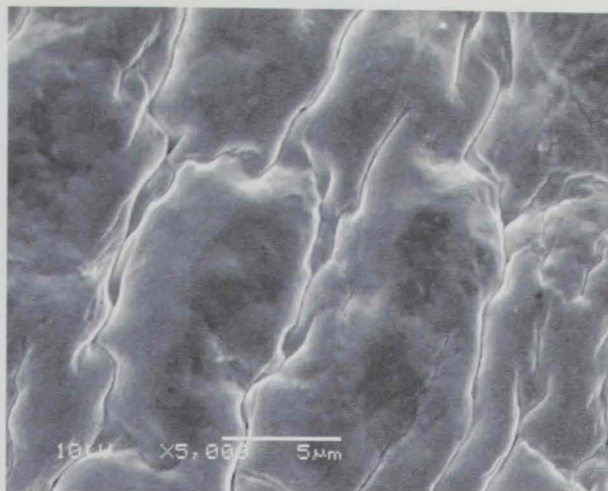


Figure 4.20b: SEM for implanted LPUPC

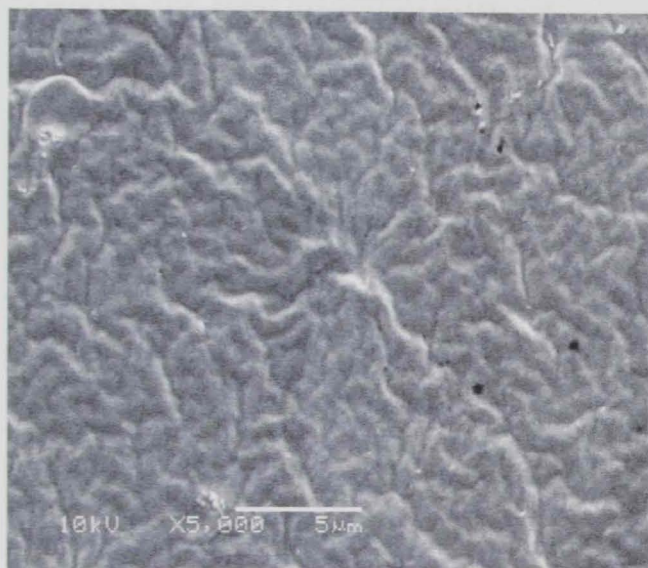


Figure 4.21a: SEM for normal MDICL4

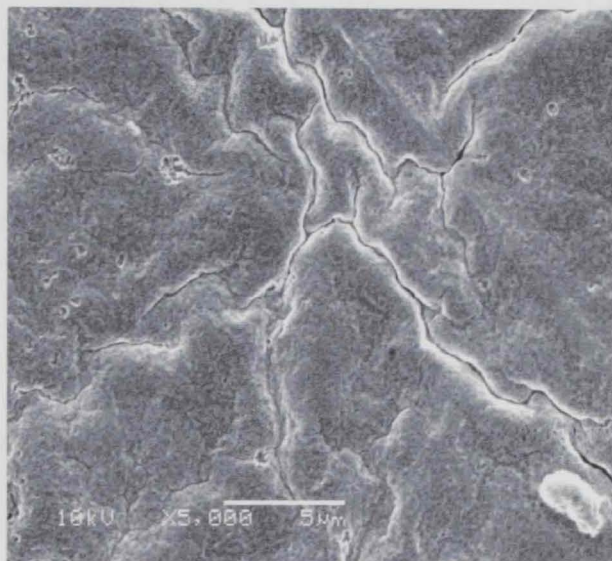


Figure 4.21b: SEM for implanted MDICL4

A comparison study was made for the sample MDICL4 before and after implantation in rat using scanning electron microscope. Figure 4.21(a,b) indicated that the surface morphology of the sample (figure 4.21a) shows a uniform distribution between the hard and soft segments.

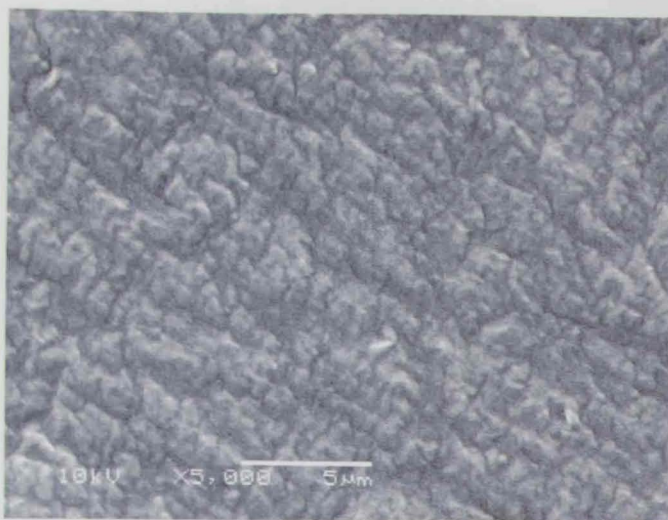


Figure 4.22a: SEM for normal MDICL8

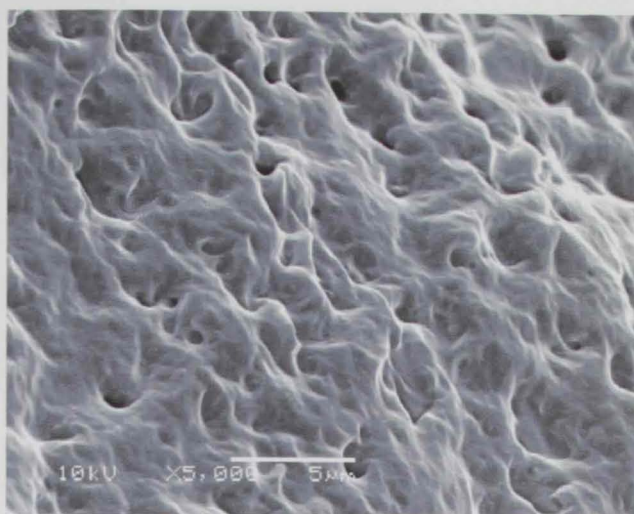


Figure 4.22b: SEM for implanted MDICL8

In relation to standard sample LPUPC (figure 4.20a) a similar distribution of crystalline and amorphous phases was observed under the same scanning magnification. In contrast to non-biocompatible material MDICL8 (figure 4.22a) notes a random or uneven distribution of very short crystalline domain.

When these samples were implanted on rats for 48 hours and then removed for surface examination, it was been found that MDICL4 sample (figure 4.21b) perform very well in comparison to LPUPC sample with no surface erosion observed in both samples (figure 4.20b and 4.21b), however there were few dust particles scattered over the surface.

Sample MDICL8 (figure 4.22b) has undergone severe erosion due to interaction between the polymer and rat skin cells. This initial observation clearly demonstrate that biocompatibility does exist in MDICL4 sample. Histology results also confirm minimum interaction with rat skin was noticeable when MDICL4 was implanted. In contrast to a severe inflammation which was noted when MDICL8 sample was implanted.

It is important to stress that these results need to be explored further to develop a full understanding of the interaction between polymer and living tissue. Again it must be

noted that these results are only primary results and final conclusion may be drawn if further studies could be carried out.



Chapter Five

Conclusions and Recommendations



Chapter Five

Conclusion and Recommendations



Conclusion:

Biomaterials have made an important contribution to modern health care. Their field of application already much more extensive than generally appreciated by the public and it is likely to expand even further as the demand for biomaterials increases. Thermoplastic linear polyurethanes (LPU) have been used in variety of medical applications, particularly at the hip and bone fixation devices. Thermoplastic polyurethane possess high strength, long-term dimensional biostability and compatibility and above all it has an excellent fatigue and abrasion resistance which makes polyurethane an excellent candidate for hip-joint replacements.

Novel thermoplastic linear polyurethane polymers have been synthesized that when compared with commercial polyurethane biomaterials offer some advantages in biostability, thermal stability and processing methodology. The synthesis of these polymers was performed via two methods, namely one shot and two shot process, to control the distribution of the soft and hard segments. The organic soft block aliphatic polycaprolactone diols with varying molecular weight, while the hard segments consist of mainly aromatic 4,4'-diphenylmethylene diisocyanate (MDI). Chain extender 1,4-butanediol was used. Different ratios of the above three components were used to produce polymers with varying soft / hard segments contents.

The synthetic route was optimized in such a way, it can be utilize for large-scale production, if the stechochemistry could be controlled. Scale-up process to produce large quantity polymer is suited for bulk polymerization which required adequate mixing of ingredients using either one or two shot process. Polymer production was reproducible with little or no batch-to-batch variation in the physical and thermal properties, but materials purification is important particularly for the MDI. No other chemicals were

added to the reaction pot and the polymer product was purified further to remove unreacted –if any- monomers.

The chemical structure of the thermoplastic polyurethane with varying degree of soft / hard segment were investigated using Fourier Transform Infra Red (FTIR) and Nuclear Magnetic Resonance (^1H NMR), while thermal properties were examined by Thermogravimetric Analysis (TGA) and Differential Scanning Calorimetry (DSC). The hardness of the samples was also examined.

^1H NMR and FTIR were used to confirm the chemical structure of polyurethanes in which the protons of urethane were observed at 7.0 ppm. The aromatic protons from MDI showed at 7.18-7.2 ppm.

The structure of the polyurethane was also verified by FT-IR spectroscopy. The absorption bands around 3333 cm^{-1} (urethane N-H stretch) and 1731 cm^{-1} (free urethane C=O). The linkage at 1067 cm^{-1} (C-O-C) stretch showed the formation of the urethane linkage.

Differential Scanning Calorimetry (DSC) was used to determine molecular organization changes such as phase segregation between soft and hard segments. On the other hand, both the mechanical and thermal properties of polyurethanes can be affected dramatically by phase mixing or phase separation. Interaction between the soft and the hard segments can increase the glass transition temperature (T_g) of the soft segment and decrease the T_g of the hard segments. The T_g of the soft segment was estimated to be below ambient temperature $\approx 45^\circ\text{C}$. The melting temperature of the soft segment was observed at around $150 - 170^\circ\text{C}$ depending on the degree of crystallization and the curing process during the synthesis. The thermal stability of segmented polyurethanes was investigated using Thermogravimetric analysis from 25°C to 700°C in air. The 5 % weight loss in air is at around 310°C , almost identical for samples with similar soft

segment content. Thermal stability is more dependent on the stability of the urethane bond, which is the weakest linkage in the polyurethane structure

A simple biocompatibility experiment was carried out using histological examination of the rat skin after implantation of polyurethane samples. A comparison study was performed with a controlled experiment using commercial polymer. The result was encouraging and no inflammatory or adverse effect to the skin was observed. Scanning Electron Microscopy (SEM) results for polyurethane samples showed that the LPUPC and the MDICL4 samples were similar in their effect without severe surface erosion. While MDICL8 sample had undergone a wide spread erosion due to the skin interaction with the polymer sample.

This research provided valuable evidence about the feasibility of producing biomaterial in particular thermoplastic linear polyurethanes on a large-scale, with excellent physical and thermal properties. This research also showed that the polymer produced has biocompatibility comparable to that obtained commercially.

Recommendations:

Based on the results of this thesis, we concluded that the effect of polyol and its ratios i.e. soft / hard segment contents, plays a major role on the thermal and physical properties of the polymer. Therefore, it is recommended to explore the possibility of using other polyols such as polytetramethylene adipate or polydimethylsiloxane with different molecular weights to produce polyurethane with high degree of linearity. Also it is recommended to examine the biocompatibility of these polymers on similar fashion as explained in this work. Comparison with commercial product is also required.

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إن الاستنتاج الأساسي هو أن بعض عينات البولوي يورثان ذات التوزيع المنتظم بين المقاطع الصلبة و المرنة أظهرت أقل تأثير طبي سلبي. عينات أخرى مبيبت تحسس مثير في الأنسجة و الكثير من التآكل السطحي في عينات البوليمر. و يمكن ربط هذه النتائج بتكوين البولوي يورثان و طريقة التحضير لهذه العينات.

وقد تم الاستنتاج من نتائج التجارب أن خواص عينات البولويوريثين تعتمد على التركيب الهيكلي الذي يختلف باختلاف التكوين. وقد وجدت أن عينتان من البولويوريثين متطابقة طبياً و عينة واحدة غير متطابقة نظراً للاختلاف التباين بين التركيبين.

الخلاصة

لقد استعمل البولوي يورثان الطبي (وهو أحد أنواع البوليمرز) في ترميم و تدعيم الجسم البشري بنجاح كبير. اختيار أي مادة للقيام بأي عمل أو استبدال أي عضو من أعضاء جسم الانسان يعتمد عادة على استجابة الجسم لمادة البوليمر و على الخصائص الميكانيكية و الحرارية للبوليمر و على النسب التركيبية من المواد النشطة التي استعملت في تحضير ذلك البوليمر.

يتكون عدد كبير من البولوريثينز المستخدمة في التطبيقات الطبية من مادة البولوي إستر و التي لا يمكن استخدامها داخل الجسم لفترات طويلة نظراً لقابليتها للتحلل المائي. البعض الآخر من البوليمرات الطبية النافعة للاستخدام داخل الجسم مكونة من مادة البولوي إيثر و التي قد تتعرض الى حد ما للتفسخ البيئي (ESC) مما يؤثر سلبياً على الخواص الميكانيكية للبوليمر على المدى الطويل.

هذا التدني ناتج عن مهاجمة الانزيمات للبوليمر ، انزيمات أفرزت من قبل خلايا دفاعية ميكروسكوبية و التي بالتالي هي جزء من المناعة الجسدية لمقاومة المواد الغريبة. هذا التفسخ حين يبتدئ قد ينمو و يمتد و قد يؤدي الى انهيار جهازي تام. ومما يتبين ظهوره كحل لهذه المشاكل هو البولوي كاربونيت بولي يورثان التي أثبتت مقاومتها للتفسخ البيئي.

و قد وجدت البولوريثينز تطبيقات في مجالات كثيرة منها في الأجهزة الطبية وتوصيل الأدوية العلاجية وصمامات القلب ومساعدات التبول وغيرها. وأهم تطورها في هذا المجال هو استعمال البولوريثينز في تصنيع المفاصل الاصطناعية. معظم هذه التطبيقات يعتمد على الخصائص المتميزة و التي من الممكن الحصول عليها من خلال السيطرة على عملية البلمرة المحكمة. البولوي يورثان المكون من بولي كاربونيت يعتبر بمثابة مقطعين متصلين كيميائياً حيث إن أحدهما صلب و الآخر مرن و مترتبة على شكل متبادل . معظم خواصه الكيميائية والفيزيائية تعتمد اعتماد كلياً على طبيعة ونسبة الفصل بين المقطعين الصلب والمرن.

أحدى مميزات البولوي يورثان المهمة هي أنه بالاستطاعة تحضيره بخواص معينة و ذلك بتغيير نسبة المكونات الأساسية للتركيب الجزيئي للبوليمر (المقطع البلوري و الغير منتظم الشكل) وذلك دون اللجوء الى استعمال الحوافز أو المليات أو المواد المضافة أو العوامل المقوية.

في هذه الدراسة لقد تم تحضير مادة البولوي يورثينز الخطية متعددة التركيبات بناء على نسبة المقاطع الصلبة / المرنة بكميات مختلفة و ذلك باستعمال ام دي أي (MDI) و بيوتين دايبول (BD) كمطيل للسلسلة وبولي كابرو لاكتون (PCL) مختلف الأوزان الجزيئية. و قد تم أيضاً تشخيص الاختلاف في خواص البولوي يورثان المحضر باستخدام التحاليل الوزنية الحرارية (TGA) ، و الأشعة ماتحت الحمراء (FTIR) و الرنين المغناطيسي النووي (NMR) و المسح التفاضلي السعري (DSC).

لقد تم فحص التطابق الطبي لبعض عينات البولوي يورثان من أجل معرفة إذا ما كانت مناسبة للاستخدام الطبي المستهدف في جراحة تبديل المفاصل على سبيل المثال. وتم تحليل النتائج باستخدام المسح الإلكتروني المجهر (SEM) لعينات البولوي يورثان و البصريات المجهرية (OM) للأنسجة البيولوجية.



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عمادة الدراسات العليا
برنامج علوم و هندسة المواد

تحضير البولي يورثان الطبي لدراسة العلاقة ما بين تركيبه و خصائصه



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رسالة مقدمة لعمادة الدراسات العليا
ضمن متطلبات الحصول على درجة الماجستير
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